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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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COMPOSITION OF MOSQUITO LARVICIDES.

By G. MACDONALD, M.D., D.P.H., D.T.M.

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A very large number of substances have been used as mosquito larvicides, but only a few are, or are likely to be, in general use. They may be classified according to whether they are applied as surface films, as floating powders, or in suspension or solution. Only those in the first category are generally useful under all circumstances, though paris green in the second has had big advantages in special conditions. With the introduction of DDT, surface film larvicides are likely again to be the most widely used ; a preliminary understanding of the properties of films is essential to their proper selection and use.

Oil Films.

An oil film, whether used as a direct larvicide or as a vehicle for another such as DDT, must have certain qualities of spreading power and stability, and if used alone it must also be toxic to larvae. The "spreading pressure", expressed in dynes per cm., is a measure of the force exerted by a film to overcome resistance to its spread. In the case, for instance, of highly purified medicinal paraffin, it is 0 dynes/cm. and the paraffin will not spread, even on an entirely clean surface. Kerosene usually has a value of about 10 dynes/cm., gas oils of 13 to 16 dynes/cm., and they will spread on many moderately clean surfaces, but are often prevented from doing so by naturally occurring surface contaminations. A good larvicidal oil for general purposes should have a spreading pressure of not less than 23 dynes/cm., and if self-spreading sufficient to penetrate deeply amongst vegetation, and against most naturally occurring obstacles, is needed, oils with very high spreading pressures, of the order of 46 dynes/cm., should be used.

ADAM (1945) has described a simple field method for the estimation of spreading pressure, by opposing successive members of a series of oils with known spreading pressures against the unknown oil on a clean water surface, by which means it is possible to find the place of the unknown in the known series. The test needs few and simple materials and apparatus, terpineol, technical quality oleyl alcohol, pure medicinal paraffin, an 8-inch glass funnel, retort stands, and running water, and can be carried out in a very primitive laboratory. The main details are excerpted in this *Bulletin*, 1946, v. 43, 255.

The spreading pressure of natural oils is largely dependent on the presence of impurities exerting surface action, and it can be reinforced by the addition of "spread-aiders". Vegetable oils and fatty acids, such as crude castor oil

(1–2 per cent.) and oleic acid (0·5 per cent.), are commonly used for this purpose, but have the disadvantage that they decrease the stability of the films. Cresylic acid is without this disadvantage and may usefully be added in proportions of 0·25 to 1·5 per cent. Commercial resin is a good spread-aider, a concentration of 0·25 per cent. greatly raising the spreading pressure, though it has the disadvantage that it is difficult to dissolve. In the process of refining oil the spread-aiding substances tend to be concentrated in some of the by-products, which are then used to increase the spreading pressure of special larvicidal oils, which, on the whole, are of good quality. In no case should substances soluble in water, such as phenols or saponated cresol, be used, as the action is quickly reversed and soon results in a decreased spread.

MURRAY (1938) has shown that the stability of films is in part due to the qualities of the hydrocarbons constituting the oil, and in part due to dissolved polar substances, some of which increase and some of which decrease the permanence of the film. To secure maximum stability, the oil should consist of a mixture of wide and over-lapping cuts with either very high or very low aromatic content, and should not contain fats or fatty acids as spread-aiders. This quality can best be judged by an empirical field test, applying the oil under natural conditions on a windless day and rejecting any specimen which does not form a stable film lasting at least two hours.

Oils appear to vary very much in their toxicity to larvae, but in reality they vary more in rapidity than in certainty of action. MURRAY (1936) has shown that once oil enters the tracheal system, the ultimate death of the larva is almost inevitable, but may occur in a few minutes or be delayed until pupation is due. The best penetration is secured with oils of medium (200°–300°C.) boiling range, and highly volatile substances may have an irritating effect which causes the larva to avoid contact and so to escape destruction. In testing oils for this quality, a film 10 microns thick (1 cc. to 1,000 sq. cm.) should be spread on the surface of water in which there are about 50 larvae. After 30 minutes the larvae should be removed without being artificially contaminated, preferably after the water surface has been cleansed by allowing the receptacle to overflow, and the death rate should be recorded at the end of one hour from the beginning of the test, in which time a good oil should kill all larvae.

When oil alone is used as a larvicide, the object is to spread a film not less than 10 microns thick, which corresponds to 14 gallons per acre, or 0·3 gallons per 1,000 sq. ft., though in practice larger quantities up to 25 gallons per acre are commonly used. With the type of oil normally used, with a spreading pressure of about 23 dynes/cm., a film can be expected to form, but deep penetration against natural films cannot be relied on. The oil must be sprayed over the entire water surface where larvae may occur. Substitutes such as drip-cans and oil-balls may work under some circumstances, but are very unreliable.

DDT Solutions.

DDT, applied in solution as a surface film, has a minimum practical lethal dose of the order of 10 mgm. per sq. metre, *i.e.* 1·43 oz. (or 1·43 pints of 5 per cent. solution) per acre, though the dose applied is usually greater than this, of the order of 4 pints per acre. Larvae are killed fairly rapidly, and first instar larvae re-appear in a few days, but the number of larvae (particularly of fully grown ones) remains subnormal for a period which may be as long as a month. Apart from this rather unreliable effect there is no residual action comparable with that exerted when DDT is applied as an adult insecticide, and it seems that the DDT is removed from the water through a physical effect of the bottom mud complex and of suspended material (ARNOLD,

FERGUSON and UPHOLT, 1945). Conversely, UPHOLT, GAINES, SIMMONS and ARNOLD (1945) have shown that a very prolonged residual effect is exerted in water free from mud, such as the containers commonly accepted as breeding places by *Aëdes aegypti*, and that its use on this type of water may revolutionize *Aëdes* control.

Several workers have shown that effective spread of DDT solutions occurs from the point of application, and RIBBANDS (1945) has recommended the abandonment of the usual spraying technique and the substitution of discrete applications from an oil can, or similar means. In his trials, doses of 4 cc. of 5 per cent. solution produced a complete kill for a minimum distance of 25 ft. along the bank from the place of application, and in one case for 70 ft., despite the presence of moderate vegetation. He found that oils commonly used were quite effective for this purpose, but the reviewer has had failures of spread on still waters in Iran, and advocates the use of specially prepared oils with really high spreading pressures, over 46 dynes/cm., for this purpose. In one of his trials of a 5 per cent. solution of DDT in a specially prepared oil, eight discrete applications of 65 cc. destroyed all larvae in 4,000 linear feet of stagnant irrigation channels containing moderate vegetation, the total area treated being 16,250 sq. ft. and the overall dose 2·5 pints per acre. Solutions in other oils applied to very similar waters failed to penetrate natural obstacles and left many living larvae.

If the full advantage of DDT is to be utilized, this method of discrete application must replace spraying. Much experience with it is to be gained before the technique can be accurately laid down, but as a working basis for extensive trial it is suggested that a 5 per cent. solution of DDT, in a stable oil with a spreading pressure of not less than 46 dynes/cm., should be used, and that on still water it should be applied in individual doses of about 2 oz., which should be sufficient to destroy larvae over an area of about 2,000 sq. ft. (the area of a circle of radius 25 ft.) from the point of application.

During the war there has been a very rapid development in the distribution of DDT solutions from aircraft. The strength of solution, the solvent, and the dose are much the same as in the case of ground application. Various types of apparatus have been used; in the simplest the stream of solution leaving a controlled outlet is shattered into a mist by the violence of the air current it meets on emergence; in others the solution is discharged into the exhaust, and a fine aerosol is thereby produced. Designs of apparatus have been developed in the normal secrecy of war, and the reviewer does not know of a published description of the type he considers suitable. With most techniques the lethal swathe is about 200 ft. broad. As one ton of solution is sufficient for 450 acres, or for a 200-ft. swathe some 18 miles long, very large areas can be quickly and effectively treated, with the additional advantage that such of the solution as falls on vegetation serves as a residual insecticide to destroy ovipositing adults; there is immediately a great reduction in mosquito density —a point emphasized in the work of LINDQUIST and MCDUFFIE (1945). The cost of maintenance of aircraft of the types commonly used in the war is so high that the techniques cannot be widely used in peace time, though apparatus for smaller aircraft may be developed for the treatment of large water areas.

Floating Powders.

Floating powders as larvicides were first advocated to take advantage of the special feeding habits of anopheline larvae, which skim minute particles from the surface. For this reason the powders are destructive to anophelines only, and are generally useless in moving water, from which they may disappear before being ingested. Paris green has become recognized as the most

generally suitable of such larvicides, though many others, such as copper cyanide, copper arsenite, and calcium arsenite, have been quite extensively used. Pure paris green contains 56·6 per cent. of arsenic as As_2O_3, and commercial samples should contain nearly this amount, preferably over 53 per cent. and certainly never less than 50 per cent. The particle size is important as only the smaller particles are ingested. METCALF and HESS (1944) showed that the average maximum sizes of particles ingested by *Anopheles quadrimaculatus* larvae were 29, 51, 68 and 106 microns for 1st, 2nd, 3rd and 4th instar larvae. It is usual to specify that all the paris green should pass through a 200-mesh bolting cloth, and that it should leave very little residue on a 300-mesh bolting cloth. Paris green answering such a specification contains many particles of excessive size, and most of the particles may be too large for ingestion by 1st stage larvae; better results may be secured with very finely powdered preparations in which most of the particles are about 2 microns in diameter. For aircraft distribution, however, very finely divided paris green is too liable to be drifted away by gentle breezes, and a slightly coarser material is required. Metcalf and Hess recommended a quality in which 84 per cent. of the particles were between 20 and 50 microns in diameter. As there may be other unappreciated factors which affect its utility, it is usual to specify that samples should be submitted for laboratory trials to verify their lethal effect.

It is very difficult to assess the minimum lethal dose of paris green owing to the difficulty of ensuring complete and even distribution of minute quantities. With a product of good quality, carefully and evenly distributed by a skilled worker, a complete kill can be obtained with doses of about 4 oz. per acre, but this is so wasteful of time that in practice a dose of 1 lb. per acre, which allows for some irregularity of distribution, is now commonly accepted.

The whole trend of practice has been to emphasize the importance of simplicity of technique, and the advantages of hand distribution over the use of mechanical sprayers in the treatment of all water except extensive swamps, and even in the latter case the simpler technique should be used unless the labour is highly skilled. For hand distribution the strength of the mixture should be 1 per cent., and any dry dust or powder may be used as a diluent, the mixture being made in a bucket with the aid of two measures to hold 1 oz. of paris green and 99 oz. of dust, respectively, and a wooden stick as a mixer. The mixture is then scattered by hand, one normal handful being adequate to treat a circle of 4 ft. radius.

Where the extent of the water to be treated makes the use of mechanical "dust guns" inevitable, a 5 per cent. dilution of paris green in some extremely fine powder, preferably powdered soapstone or "soft stone", should be used, the mixture being made if possible in a cement mixer at some central site and distributed ready mixed to the place of application. It has been common to use a 33 per cent. mixture for aircraft distribution, but when this is indicated, DDT has such manifest advantages that the use of paris green will probably now come to an end.

Emulsions and Suspensions.

A number of substances have been used in emulsion form as larvicides, phenol in the original Panama larvicide, cresol, pyrethrum, and now DDT. None of them has permanently established itself for general use, and probably none will. In the case of DDT the tendency has been to make a 5 per cent. solution in fuel oil and to emulsify this with an emulsifying-spreading agent (unfortunately always described under a proprietary title) in about 30 times its volume of water, thereby producing a larvicide to be used in doses comparable with the dose of oil—15 to 25 gallons per acre. The method may

save some of the material cost of oil, it saves none of the labour which is the chief cost of oil distribution, and self-spreading, such as described for DDT surface films, cannot be relied on. The method may be of special use in the treatment of minute breeding places, such as those of *Aëdes*, where applications of oil solutions of DDT might be very wasteful, in which case the dose is arranged to secure a final dilution of about one part DDT per million parts of water.

When liquid-based paris green was introduced by BARBER, RICE and MANDEKOS (1936) it was carried in the oil phase of a kerosene-water emulsion and was particularly suitable for the treatment of small breeding places, including those in which the water was running. AZIZ (1939) later developed the use of plain suspensions of paris green in water, and until the introduction of DDT this remained the most effective method for the treatment of shallow moving water in places where transport difficulties made the carriage of oil impossible or unduly expensive. The paris green, which should be of normal grade, and not the extremely fine grade referred to above, is mixed with water in the spraying machine from which it is to be applied, in sufficient quantity to give a 1 in 500 or 1 in 250 suspension, which is kept evenly mixed by occasional agitation of the machine. It is sprayed on the breeding place in sufficient quantity to give a minimum of 1 part, or preferably 1·5 parts, of paris green per million of water, that is, for a 1/500 suspension sprayed on water 3 inches deep, one gallon to 870 sq. ft. It has proved itself of exceptional value in the treatment of the shingly streams commonly used as breeding places by *Anopheles superpictus* in the Mediterranean area, though recent experience suggests that DDT solutions may largely replace it.

Each of the larvicides described has some special qualities which make it more or less suitable for use for different kinds of breeding places, or in different circumstances, and each of them will probably remain in wide use. In any one scheme of mosquito control it is desirable to use the minimum possible number of methods, and preferably one method only. To this end the method which is most generally suitable for the common conditions locally encountered should be chosen and adapted to as many of the local conditions as possible, even though it may not theoretically be the most desirable for all of them. Only by this selection of methods can the proper training of subordinate labour, on whom success finally depends, be secured, and the occasional use of a method which may not locally be the most economical is preferable to the confusion which arises when a choice of methods is left to men unqualified to make it.

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SUMMARY OF RECENT ABSTRACTS.*

VIII. TYPHUS GROUP OF FEVERS.

General.

GEAR (p. 362) gives an account of the rickettsial diseases of South Africa. Louse-, flea- and tick-typhus are widespread, and the last can usually be distinguished from the other two clinically and by the Weil-Felix reaction.

WOLSTENHOLME and GEAR (p. 877) discuss the various serological tests used in the differentiation of fevers of the typhus group. Most reliance is placed, for various reasons, on the complement fixation reaction, but, as pointed out by MEGAW in comment, this test does not always distinguish epidemic from murine typhus, though it is usually effective in the diagnosis of the tick-borne group. [See also PLOTZ *et. al.*, below.]

BENGTSON (p. 983) sums up the experience of the complement-fixation test in the rickettsial diseases. She thinks it highly specific; it can be used in retrospective diagnosis and in rats, and may become a routine procedure, complementary to the Weil-Felix reaction.

FITZPATRICK (p. 982) reports a study of the rickettsia agglutination test in the diagnosis and differential diagnosis of epidemic and murine typhus, and Rocky Mountain spotted fever. The test is capable of distinguishing between epidemic and murine typhus, usually by a difference in titre of the reaction to the two antigens; differentiation of these from Rocky Mountain fever is more clear-cut. Details should be sought in the original abstract.

BLANC and BALTAZARD (p. 714) have carried out extensive research into the question of immunity in fevers of the typhus group. A frank attack of epidemic or of murine typhus immunizes against both infections for at least several years. Rocky Mountain spotted fever and boutonneuse fever also immunize against each other. Inapparent infection produces immunity, and inapparent reinfection must be very rare. Hereditary transmission of infection in ticks readily explains persistence of the tick-borne fevers, but this does not occur in lice or fleas. The same authors (p. 715) state that of the two groups of typhus fevers, louse-borne and flea-borne on the one hand, and tick-borne on the other, neither can be transmitted by the vectors of the other. Murine rickettsiae can, however, be transmitted by lice from man to man. They do not think that inapparent attacks are important in maintaining louse-borne typhus during inter-epidemic periods, but think that infection from dried, infected, louse faeces is the cause of sporadic attacks, and may initiate epidemics. Infected louse faeces are quickly inactivated by moisture, and sterilization of clothing by steam is reliable. Louse control, by itself, is inadequate as a means of checking epidemics.

EYER and RUSKA (p. 23) have studied the morphology of rickettsiae by means of the electron microscope.

DARZINS (p. 544) describes a method of staining rickettsiae, details of which should be sought in the original abstract.

Vaccination.

SCHULTEN (p. 27) quotes figures which indicate that typhus in previously vaccinated persons is milder and of shorter duration than in unvaccinated controls. BILIBIN (p. 796) notes that in persons vaccinated against typhus the onset of the disease, when it occurs, is rapid, but its course is usually mild. Diagnosis may be difficult.

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* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

DURAND *et al.* (p. 107) tested the sera of a group of people in North Africa, before and after inoculation of various vaccines, by means of a protection test in which infective material was mixed with the serum and then injected into the skin of rabbits. Some of the sera gave protection before vaccination, but many more after vaccination. Killed vaccines appeared to be more effective than live.

From experience of vaccinating mice, FITZPATRICK (p. 793) concludes that the toxic factor in epidemic and murine strains of rickettsiae is identical.

LEVKOVICH and PETRISHCHEVA (p. 268) find no difference in effectiveness between vaccine of the Cox type, mouse lung vaccine, and vaccine prepared from lice, except that one prepared from the whole bodies of lice may cause allergic skin reactions. They give details of their methods of dealing with the lice.

DONOVICK and WYCKOFF (p. 792) show that by the end of 1942 certain improvements had been made in the preparation of typhus vaccines, which rendered them more effective, and that the titre of the complement fixation reaction in guineapigs is a reliable indication of vaccine potency. They (p. 882) give information on the techniques employed in preparing these vaccines.

In a discussion at the Royal Society of Medicine (p. 979), STUART-HARRIS remarked that all typhus vaccine used in the British Army since 1943 was of the Craigie type, and FULTON made the point that when vaccines were standardized by counting the rickettsiae, it was found that animal-lung and yolk-sac vaccines gave similar degrees of protection. FOX knew of no authentic case in the Allied Forces of a person dying of typhus after having been properly vaccinated with the Cox-Craigie vaccine.

GALLARDO *et al.* (p. 23) describe their experiences in the preparation of typhus vaccine by the Cox method.

TOPPING and SHEAR (p. 457) have shown that the supernatant fluid from a centrifuged suspension of epidemic typhus rickettsiae grown in yolk sacs contains a substance having the same immunological properties (complement-fixation and production of immunity in inoculated animals) as the rickettsiae themselves. This substance is probably soluble, but may possibly be contained in very small rickettsiae. [See also GIROUD, below.]

ROTH (p. 719) reports reactions to typhus vaccine, which are probably due to residual egg antigens.

Information on delousing and immunization against typhus is contained in the *Monthly Bulletin of the Ministry of Health* (p. 879). This note was intended for the information of medical men in Britain.

HORRENBERGER and RENOUX (p. 107) and SERGENT and HORRENBERGER (p. 365) show that sheep and goats can be used in place of rabbits for the preparation of animal-lung typhus vaccine.

By adding sterile sulphathiazole to the suspensions of infected mouse lung used in making intranasal transfers, RUIZ CASTAÑEDA and ROBERTO SILVO (p. 193) have been able to check secondary infections due to Gram-positive organisms, and have made 74 successive transfers of two strains of *R. prowazeki*. This has proved to be of great value in the preparation of bivalent vaccine.

RUIZ CASTAÑEDA and SILVA (p. 457) describe experimental work which indicates that animal-lung vaccine from animals infected intranasally by both epidemic and murine rickettsiae (bivalent vaccines) are more effective against subsequent infection with epidemic strains than vaccines of epidemic origin alone.

GIROUD (p. 366) shows that rickettsiae may remain alive in infected animal lungs kept at −25°C. for 14 months. There was no indication that the rickettsiae could undergo attenuation while preserving antigenic power.

GIROUD (p. 366) has demonstrated experimentally that lung tissue in which there has been heavy growth of rickettsiae, but from which the rickettsiae have been removed, possessed good antigenic properties and is effective as a vaccine.

VAINBERG *et al.* (p. 549) show that the incidence of typhus in a group of medical employees, who had been inoculated with a Russian mouse-lung vaccine, was considerably lower than that in a comparable control group. A similar finding in other groups of people particularly exposed to infection is reported by RAVIKOVICH *et al.* (p. 549). When it occurred in the vaccinated, the disease was relatively mild. FAIERSTEIN (p. 456) has used a formalin vaccine from mouse lung preparations for vaccinating employees of the underground railway in Moscow. The protection afforded was moderately good.

OSBURN (p. 455) describes the preparation of an alum-precipitated vaccine from the peritoneal washings of South African gerbils infected with *R. prowazeki*. In spite of certain anomalous findings in the animal tests with this vaccine, it appears to have some advantage over non-precipitated vaccines with which it was compared.

LEMAIRE (p. 268) states that the live vaccine of Blanc can be kept for an indefinite period when stocked in dry form *in vacuo*. It was used on a large scale during an epidemic of typhus in Algiers, and the case incidence and fatality in the unvaccinated were 8 times and 5 times as high, respectively, as in the vaccinated.

CLAVERO and PÉREZ GALLARDO (p. 794) have used a "non-pathogenic and immunizing strain of *R. prowazeki*" as a vaccine, both in the living state and after desiccation. No serious reaction occurred in 2,217 persons vaccinated, except in one, who had what might have been regarded as a mild attack of typhus. The Weil-Felix reaction becomes positive in almost half of those vaccinated. No estimate of the protective value of this vaccine is given.

BERGER and BRZEZINSKI (p. 986) have shown that the addition of petrol-ether extracts of liver, or certain fatty acids, to suspensions of rickettsiae has a pronounced antitoxic and antirickettsial effect.

BRAUN and UNAT (p. 108) have shown that intravenous injections of killed *Proteus OX19* provoke positive Weil-Felix reactions to the same organism, and argue that mixed vaccines of rickettsiae and *Proteus*, administered intravenously, may be more effective than rickettsial vaccines given subcutaneously.

Proteus OX19 type. Vectors: louse and flea.

Louse typhus.

Epidemiology.—HUSSAIN (p. 881) notes that louse-infestation, and typhus, are common in the highlands of Kashmir, and JACKSON (p. 881) also refers to typhus in this area.

SOFIA and SPADARO (p. 547) claim that both the murine and the classical type of typhus exist in Asmara, Ethiopia.

Aetiology.—ELFORD and VAN DEN ENDE (p. 455) have studied the viability and filterability of typhus rickettsiae; for details the original should be consulted.

ANDERSON (p. 106) has experimented on the survival of *R. prowazeki* in milk, water and other fluids.

COHEN and CHARGAFF (p. 192) have made highly technical studies of the composition of *R. prowazeki*.

A heat-labile toxin separable from the rickettsiae of epidemic and murine typhus has been studied by KLIGLER and OLEINIK (p. 23).

GIROUD and PANTHIER (pp. 104, 985) have shown that the rickettsiae of louse-borne, epidemic typhus may behave either as orchitic or non-orchitic strains according to the conditions in which they are transmitted by intraperitoneal inoculation in guineapigs. They have now failed to infect rats by

intraperitoneal or lung inoculation of three epidemic strains maintained in rabbit lung passages, and conclude that the rat is a sure test for the differentiation of epidemic and murine rickettsiae.

PSHENICHNOV (p. 269) infects lice by allowing them to feed, through animal membrane, on defibrinated human blood, to which an emulsion of infected louse intestine or guineapig brain has been added. The method of handling and rearing the lice is described by RAÏKHER (p. 270). SNYDER and WHEELER (p. 987) have devised a technique for feeding lice on rabbits, and for infecting them with typhus by this means. Infection of the lice occurred if they were fed shortly after the rabbit was inoculated, but if fed 117 hours after inoculation, the results were negative. If proper precautions are taken lice may be used for the isolation of rickettsiae from patients [see LASKIN, below].

Transmission.—BLANC and BALTAZARD (p. 715) demonstrated that human volunteers did not become infected when bitten by infected lice whose faeces were prevented from touching the skin. The natural reservoir of rickettsiae is infected louse faeces. GROMASHEVSKY *et al.* (p. 460), however, contend that the only sources of infection in typhus are patients suffering from the clinical forms of the disease, and the lice which have fed on them. If the spread of the disease has really been terminated, it cannot again begin unless fresh cases are introduced into the community. [The authors do not support the view that inapparent cases occur, and, evidently, do not think that infection occurs from the inhalation of dried, infected, louse faeces, which, in North Africa and elsewhere, has been regarded as a likely source of renewed outbreaks (see PSHENICHNOV, this *Bulletin*, 1944, v. 41, 836).]

TOKAREVICH (p. 460) describes five laboratory infections with *R. prowazeki*, two by droplet infection, two by contamination of mucous membranes by infected louse faeces, and one by inoculation. Two of the patients had been vaccinated, and the author points out that this experience was in contradiction with the consistently negative results previously obtained when feeding infected lice on vaccinated persons. The reason is perhaps related to high dosage or to maturity of the rickettsiae in these accidental infections.

By injecting into animals material from the nose, mouth and trachea of patients with typhus, with negative results, DING (p. 22) has shown that there is no direct evidence that transmission of infection from man to man can occur by droplets from the respiratory tract.

LINSKIS (p. 988) reports a case of typhus contracted as a result of blood transfusion from a donor who was in the incubation period of the disease.

BLANC and WOODWARD (p. 547) have shown that the monkey louse *Pedicinus albidus* can become infected by epidemic typhus, and that injection of ground-up infected lice will transmit the disease. They have not proved that these lice can transmit typhus in natural conditions.

Pathology.—RANDERATH (p. 458) describes post-mortem findings in typhus. Typhus nodules were never found in the heart, which, however, showed a condition of typhus myocarditis. Circulatory failure was believed to be due to damage to the vasomotor centres, and to be associated with the condition of the peripheral vessels rather than with myocarditis [see also the findings in scrub typhus, below]. The most striking complication was diffuse haemorrhagic glomerulo-nephritis.

DURÁN (p. 458) describes the Fraenkel nodules of typhus; he regards the fundamental lesion of typhus as an endothelial necrosis, of varying intensity.

GOLDEN (p. 718) gives a description of the morbid anatomy of typhus, details of which should be sought in the original abstract.

AVTSYN (p. 266) describes the pathological changes in the lungs of mice inoculated intranasally with suspensions of typhus rickettsiae.

Tests.—LASKIN (p. 795) claims that examination of the gut of lice collected from typhus patients affords a good method of early diagnosis before the Weil-Felix test is positive. Typhus rickettsiae are present, and can easily be distinguished from non-pathogenic rickettsiae.

DE LA CAMARA (p. 984) reports an outbreak of typhus in Spain, but notes that the results of the Weil-Felix test were irregular. In comment, MEGAW emphasizes the importance of standard strains of *Proteus*, and standard technique, in such tests.

FROMME and GAASE (p. 197) have tested the specificity of the Weil-Felix reaction by the examination of a large number of sera obtained for tests for syphilis. They conclude that if a titre of 1 in 200 is accepted as a minimum, non-specific reactions occur in only 1·2 per cent. of apparently uninfected persons. They conclude that in persons vaccinated against typhus, and in those who have been living in infected communities, the reaction may be positive, possibly as a result of inapparent attacks.

SCHRÖER (p. 545) maintains that if the reagents of the Weil-Felix test are incubated together for 2 hours and then kept for 22 hours at room temperature, the results in typhus are more clear-cut, and there is no tendency for false positive results to develop in other diseases. The contrary view, however, is expressed by WINKLE (p. 545). The latter author (p. 546) discusses three Russian patients from the Far East, who gave reactions to *Proteus OXK*, and one German soldier who gave the same reaction, probably as a result of infection of a wound with a strain of *Proteus*.

NELSON and CRUICKSHANK (p. 363) have been unable to confirm the findings of GRATCH, that the sera of pregnant women agglutinate *Proteus OX19*, constantly and at high titres. Similarly, HOARE (p. 794) failed to confirm the findings of Gratch.

BRUMPT (p. 197) describes a slide test, with a suspension of *Proteus OX19* stained with methylene blue, and in which a drop of the patient's blood is used, which gives results comparable with those of the Weil-Felix reaction. The test is rapidly performed, and if it is done on photographic paper, a permanent record may be obtained and kept.

VARELA (p. 364) thinks that the fact that guineapigs infected with typhus do not give a positive Weil-Felix reaction is due to the presence of an antigen in their tissues which is related to the antigen in *Proteus*.

COHEN (p. 981) has studied the chemical alteration of bacterial surfaces, with special reference to the agglutination of *Proteus OX19*; the paper should be read in original.

VAN ROOYEN (p. 194) has performed the rickettsia-agglutination test, in 323 cases of typhus in the Middle East. In Egypt, Iraq and Iran the results indicated that the epidemic strain was most common, in Palestine the murine. When the epidemic reaction was positive at higher titre than the murine, the case was regarded as of epidemic, louse-borne type, and when the murine titre was higher, as of murine type, but information regarding the epidemiological conditions is seldom sufficient to justify an opinion as to which vector was concerned in a particular case. Moreover, in nearly 40 instances there was only moderate difference between the titres. Some cases suggested tick-borne typhus, and it is possible that this form exists there. Captured rats gave the murine reaction. The author prefers a classification by vector and would avoid the use of the words epidemic and endemic in relation to typhus. Another account of the same work has been written by VAN ROOYEN *et al.* (p. 264).

RUIZ CASTAÑEDA (p. 716) has used the rickettsia agglutination slide test in differentiation between epidemic and murine typhus, with success in that agglutination of the homologous organism occurs at higher titre than that of the heterologous organism. Nevertheless, cross agglutination does occur,

especially with anti-murine serum and epidemic rickettsiae, which indicates that murine rickettsiae contain more of the epidemic antigen than *vice versa*. This may explain the greater cross protection from murine than from epidemic vaccines.

BRIGHAM and BENGTSON (p. 552) show that the complement-fixation test is a much more sensitive test of the occurrence of typhus in rats than the Weil-Felix reaction. They support this conclusion by a large body of evidence.

WERTMAN (p. 635) makes the point that when relatively crude egg-yolk cultures of rickettsiae are used as antigens for complement fixation tests, a non-specific antigen from the yolk is present and may give false positive reactions, especially with Wassermann-positive sera, and still more with the particularly sensitive technique of incubation for 18 hours at 4–8°C. This antigen can be removed by repeated washing and centrifugation.

DAMON and JOHNSON (p. 990) prefer to carry out the complement-fixation test at ice-box temperature overnight, rather than at 37°C. for one hour.

SILVA-GOYTIA (p. 718) has used the complement fixation test in Mexico, and concludes that the typhus there is very largely of epidemic type, but that there are some cases of murine origin.

SMORODINTSEV and DROBYSHEVSKAYA (p. 196) have devised a complement-fixation test for typhus, designed to detect in the patient's serum an antigen which is present in the early days of the disease, but which is gradually neutralized by antibodies developed by the patient, so that by the 10th day it cannot be detected. Inactivated serum from the patient is mixed with inactivated convalescent serum (which presumably contains the antibody) and with titrated complement. This mixture is kept at 0·2°C. for 18 hours, and the sensitized red cells are then added and incubated at 37°C. Hyperimmune rabbit serum would probably give more satisfactory results than convalescent human serum. SMORODINTSEV and FRADKINA [this *Bulletin*, 1944, v. 41, 1021] had previously described a rapid slide-agglutination test for the detection of this antigen; if these two tests are confirmed, their value in diagnosis in the early stages of the disease are sufficiently obvious.

LEÓN (p. 984) notes that the complement-fixation test, with an antigen prepared from *Proteus OX19*, is more sensitive than the Weil-Felix reaction.

GIROUD (p. 199) uses a skin-sensitivity test for typhus, in which an animal-lung antigen is employed. A positive result is obtained after an attack of the disease, or after successful vaccination, and indicates a state of immunity. A negative result is an indication for vaccination; it may occur in debilitated persons even after an attack of the disease. BISCHOFF (p. 198) describes an intradermal test carried out with weak Weigl vaccine. A negative result is given in unvaccinated patients with typhus, during the course of the disease and for 15 days afterwards, and is taken to indicate the presence of specific neutralizing antibodies.

Clinical features.—Clinical features of cases of louse-borne typhus are described by SINGH (p. 24). The outbreak occurred in the Persia-Iraq Field Force in 1943. ALCANTARA (p. 988) describes the clinical features of typhus, pointing out that the mildness of the disease in children, which often causes it to be missed, is important epidemiologically. WU and CHI (p. 795) note the relative mildness of typhus, probably louse-borne, in South China.

WOODWARD and BLAND (p. 199) have studied the cardiovascular system in typhus. They conclude that the abnormalities are due chiefly to the foci of necrosis in the smaller vessels, and that there is little evidence of cardiac weakness. Renal damage is rare, and the oliguria (in spite of large fluid intake) can be corrected by giving chlorides and overcoming dehydration. In treatment, careful nursing and adequate fluid and supporting foods are needed; cardiac stimulants were not indicated in any case in this series. SIEDEK *et al.*

(p. 105) found evidence of cardio-vascular disorders in 45 per cent. of 500 patients with typhus, but these are apparently associated with damage to the vasomotor nerve centres and the peripheral vessels, lesions of the heart playing only a secondary part. CIMMINO (p. 106), however, has found electrocardiographic evidence of myocardial lesions.

ASCHENBRENNER (p. 104) notes that the chief cause of death in a series of cases of typhus was damage to the central nervous system. Severe myocarditis was rare. He used strophanthin in large doses during the febrile period, and in smaller doses in convalescence when evidence of circulatory disturbance persisted.

v. STOCKERT (p. 459) describes certain syndromes which result from localization of typhus lesions in various parts of the central nervous system—the midbrain, bulbar and extrapyramidal syndromes. In the first, the most important disturbance of the vegetative nerve centres is the characteristic fall of blood pressure, but it is not certain how far myocarditis is responsible for this. SCHELLER (p. 200) has contributed a discursive paper on signs and symptoms associated with the nervous system in typhus. KOVÁCS and v. KUP (p. 461) describe the clinical features of typhus, and outline a treatment which they believe to have reduced the severity of nervous symptoms and the incidence of complications.

MÜLLER (p. 548) describes the ophthalmological changes in typhus, which include the presence of typhus nodules in the retina or choroid, and retinal haemorrhages.

ASCHENBRENNER (p. 25) remarks on the very great increase in blood urea which may be a feature of typhus ; he is unable to explain it except as due to increased production of urea and diminished excretion owing to renal damage, either inflammatory or " functional."

WILCKENS (p. 266) describes the symptoms of typhus, noting that an after-fever lasting 1–2 days is relatively common. In treatment he found that administration of luminal was of some benefit. ASCHENBRENNER & MARX (p. 105) note that an unexplained rise of temperature may occur during convalescence from typhus ; they also give a list of the common complications of the disease.

RAETTIG (p. 25) describes two cases in which, he claims, true relapse occurred after attacks of typhus. In comment, MEGAW throws doubt on the diagnosis of the first febrile attack in each case. It is noted that each of these patients was treated by injection of convalescent serum, and the question arises whether each was, in fact, infected by the serum.

Treatment.—YEOMANS *et al.* (p. 201) report encouraging results in a small series of typhus patients treated with *p*-aminobenzoic acid in the first few days of the attack, and compared with a series of comparable controls. The optimum dosage is not known, but the initial dose was 4–8 gm., followed by 2 gm. every 2 hours until the temperature was normal. The drug was given suspended in 5 per cent. sodium bicarbonate solution. The effect of this treatment was to shorten the febrile period and to reduce the severity of the disease. Some of the treated patients had a secondary rise of temperature soon after the end of drug treatment ; this was not serious. The effect of *p*-aminobenzoic acid, both in inhibiting the growth of rickettsiae in yolk-sac culture, and in treatment of mice infected with a murine strain, was demonstrated by GREIFF *et al.* (p. 362). PINKERTON (p. 878) also discusses the therapeutic action of *p*-aminobenzoic acid in typhus. HAMILTON *et al.* (p. 796) describe the inhibitory action of *p*-aminobenzoic acid on rickettsiae (epidemic and murine strains) growing in yolk-sacs of fowl embryos.

LEÓN (p. 202) has used hyperimmune rabbit serum for the treatment of typhus, giving 20 cc. intravenously at intervals of 12 hours until the temperature subsides. The results were apparently satisfactory in a small series of

cases. A beneficial effect of the use of hyperimmune rabbit serum in louse typhus is also indicated by the results obtained by STEVENS (p. 364) in a small series of patients. SHUBLADZE *et al.* (p. 461) have immunized horses with infected mouse-lung preparations of *R. prowazeki*, and have used the horse sera for treatment of typhus in animals, with some success. Preliminary clinical trials in man have been promising.

Certain substances, which are described in the original abstract, were tested for activity against the rickettsiae of murine and epidemic typhus by ANDREWES *et al.* (p. 20). Activity was recognized in some of these drugs, but they proved disappointing in the treatment of human typhus. SKORIN and KORSHUNOVA (p. 638) have tested 56 compounds for chemotherapeutic activity in experimental typhus. In a critical evaluation of the many drugs which have been advocated by German medical men, BRANDENBURGER (p. 26) adopts an attitude of scepticism. He relies on careful nursing and the administration of plenty of fluid, with generous and varied diet.

Treatment by daily warm baths, injections of " artificial blood " and saline, is advocated by LAMPERT (p. 365), but the evidence of its value is not clear.

YARYGIN and NAGIBINA (p. 989) describe the method of " buxation," which consists of alternately withdrawing and reinjecting 10 cc. of cerebrospinal fluid after the patient has been given large doses of sodium salicylate. This treatment (for details of which the original abstract should be consulted) was tried in typhus, with some favourable results.

ALISOV and KOSSOVAJA (p. 989) have observed some benefit from vaccine therapy in severe attacks of typhus.

LAURE (p. 267) describes the types of gangrene seen in typhus, and the treatment advocated, which consists of infiltration of the lumbar sympathetic ganglion with novocaine, without adrenaline.

Control.—SERGENT and BÉGUET (p. 270) have used the insecticide powders MYL and DDT for delousing certain communities in Algeria. These preparations were very effective, but the authors are pessimistic on the question of complete and permanent eradication of lice, and conclude that these dusts can best be used by mobile disinfesting units when outbreaks of typhus occur.

BEACH and RENNIE (p. 880) report four cases of typhus in prisoners of war returned to England from Germany. They had been dusted with DDT and were free from lice. MEGAW, in comment, makes the point that delousing by DDT does not sterilize infected louse faeces.

Louse and flea typhus.

LEON (p. 193) argues that typhus is caused by a single species of rickettsia, of which there are two strains [? varieties], *R. prowazeki prowazeki*, and *R. prowazeki mooseri*. The former does not provoke vaginitis in animals; the latter does so. Either strain can cause endemic or epidemic typhus, and either can be of high or low virulence. The author supports his conclusion by records of his own work. In comment, MEGAW points out that although these organisms cannot be clearly differentiated by their capacity to provoke orchitis, they can be distinguished by complement-fixation and rickettsia-agglutination tests. From the point of view of control, the vector, louse or flea, is important.

SILVA and RUIZ CASTAÑEDA (p. 990), having infected guineapigs with both epidemic and murine rickettsiae simultaneously, have found that transfers through male guineapigs favour the isolation of the murine strains, and through females of the epidemic strains.

ANDERSON (p. 192) has shown that the cotton rat *Sigmodon hispidus hispidus* is as highly susceptible as the South African gerbil to infection with classical

and murine strains of typhus rickettsiae ; it has, therefore, been used in laboratory research work. Sera of infected cotton rats do not agglutinate *Proteus OX19.*

Flea typhus.

SOFIA (p. 109) has isolated rickettsiae of the murine type from man in Asmara (Eritrea), and also from the brains of wild rats. HARINGTON and YOUNG (p. 271) have isolated murine strains of rickettsiae from rats and from a patient in South Africa, near Port Elizabeth.

POLLARD and AUGUSTSON (p. 551) perform complement-fixation tests on rats, to detect evidence of murine typhus in them. They have obtained positive results in endemic areas, but not where the disease is not known to occur. Some of the rats giving positive tests were captured in theatres ; this fact may explain certain outbreaks in man.

IRONS *et al.* (p. 462) have isolated murine rickettsiae from *Ctenocephalides felis* from kittens probably connected with a human outbreak. It is possible, but unlikely, that the fleas acquired the infection from rats, and the present finding indicates that cats may be a reservoir of infection in certain circumstances.

According to evidence collected by RUIZ SÁNCHEZ (p. 272) the endemic typhus of Guadalajara, Mexico, is of murine origin. VARGAS (p. 796) has isolated a strain of murine rickettsiae from a patient in El Salvador. MACCHIAVELLO (p. 103) has studied strains of rickettsiae isolated from patients, or from lice, in Equador. One of these was regarded as a murine strain, but the other two behaved irregularly in animals. The author does not think that the terms orchitic and murine, as applied to strains of rickettsiae, are synonymous. MONTOYA (p. 551) reports an outbreak of typhus, which he thinks was murine in origin, in Colombia.

ALICATA and BREAKS (p. 271) have isolated rickettsiae from a patient in Honolulu, which were identical with a standard murine strain, and from a high proportion of rats in the area. Cats, dogs and the fleas collected from them were negative.

LIU (p. 719) has isolated rickettsiae of murine type from rats, rat fleas and lice, during an outbreak in Peiping. He thinks the human disease may have been louse-borne, but MEGAW, commenting on this, is not convinced that louse-transmission was conclusively proved.

JETTMAR and SHIGAN (p. 981) report on the Weil-Felix reaction in man and rats in Kweiyang, China.

BLANC *et al.* (p. 713) have shown that the ass-louse, *Haematopinus asini*, may transmit murine rickettsiae, and *Xenopsylla cheopis* and *Pulex irritans* epidemic rickettsiae. The fleas *X. cheopis* and *Ctenocephalides canis* do not appear to be able to transmit the rickettsiae of Rocky Mountain and boutonneuse fevers.

DAMON and JOHNSON (p. 637) compared freshly prepared rickettsial suspensions (epidemic or murine types) with commercial vaccines, in relation to their usefulness in the complement fixation test for typhus of murine type. The best results were obtained with the fresh suspension of the murine type.

ARBONA (p. 990) quotes evidence which suggests some slight favourable effect in the treatment of flea-borne typhus with mepacrine.

Proteus OXK type. Vector : mite.

MEGAW (p. 797) has contributed a comprehensive account of scrub typhus, in which he shows that during the war there has been an average case-mortality rate of 10–15 per cent., a high incapacitation rate, and a depressing psychological effect. He discusses classification, epidemiology and transmission, and in relation to the clinical findings makes the point that a necrotic ulcer is not

always present. No adequate summary of this paper, and of the comments of LEWTHWAITE, who reviewed it, is possible in brief space, and the original should be consulted. It was a timely account of an important disease.

FARNER and KATSAMPES (p. 272) have compiled a summary of available information on tsutsugamushi disease, which should be read in the original.

DE VIDAS (p. 882) describes the clinical and pathological features of scrub typhus as he saw it in New Guinea, noting that the maximum titre of the Weil-Felix reaction with *Proteus OXK* occurred 22–25 days after onset. SATHER and SILBERSTEIN (p. 885) also report on cases from New Guinea.

SINGH (p. 883) gives an account of an outbreak of scrub typhus in Burma, in soldiers who had camped in a rural area. MENON and IBBOTSON (p. 884) record an outbreak in a unit which entered a " typhus island " in N.E. Burma. Clinical features and complications are described, and treatment is outlined. The authors note that malaria was so common that a therapeutic course of mepacrine was given at the onset, in all cases.

HAY (p. 109) describes an outbreak of scrub typhus in a force of Royal Marines who landed on an unnamed coast in the Far East. These men had been working in close contact with scrub conditions. The symptoms are described, but the description should be sought in the original abstract ; primary lesions, once thought universal in this disease, were rare. Diagnosis was confirmed by agglutination of *Proteus OXK* in high titre in all cases. It was found that local inhabitants also gave positive reactions with *Proteus OXK*, and it seems probable that all local children become infected at some time, and that local adults possess some degree of immunity. Larval mites, probably *T. deliensis*, were found on trees and grasses and on rats, chiefly *Rattus rattus frugivorus* ; serological tests on rats indicated that the disease was present in them. [Later evidence (MANSON, *J. Roy. Nav. Med. Serv.*, 1946, v. 32, 105) makes it clear that this outbreak, also refered to by ZAIR (below), occurred in the Maldive Islands.]

WILLIAMS (p. 367) has published a list of mite vectors and animal reservoirs of tsutsugamushi disease. [The evidence available for some of the mites mentioned is somewhat tenuous. The mites definitely incriminated in the literature appear to be :—

Trombicula akamushi.
Trombicula deliensis.
Trombicula fletcheri (probably=*T. akamushi*).
Trombicula walchi (probably=*T. deliensis*).

In addition, *T. minor* (=*T. hirsti*) is suspected.]

BLAKE *et al.* (p. 991) made a very thorough study of tsutsugamushi disease in New Guinea. They point out that the only mite hitherto proved by experiment to be a vector is *T. akamushi*, though there is much evidence to incriminate *T. deliensis*. The only animals so far found infected in nature are the vole *Microtus montebelloi* and undetermined species of wild rats in Malaya. They isolated strains from *Trombicula fletcheri* [=*akamushi*] which were identical with those isolated from man. The Syrian hamster was found to be specially suitable for passage. The authors give descriptions of the disease in man. This long monograph should be read in original. KOHLS *et al.* (p. 993) report a continuation of the same work, in which they recovered *R. orientalis* from pools of *T. fletcheri* [=*akamushi*] and *T. walchi* [=*deliensis*]. These were taken from *Rattus concolor browni*. The rickettsiae have also been recovered from this rat.

MCCULLOCH (p. 369) makes the point that all the species of mites which occur in countries in which scrub typhus is endemic, should be regarded as potential vectors of that disease. [Such a view needs verification.] He describes their

habits and the means of controlling them. WOMERSLEY and HEASLIP (p. 28) have written a comprehensive paper on the Trombiculinae of the Austro-Malayan and Oriental Regions. No further abstract of this is possible.

From his experience of three outbreaks of scrub typhus, COOK argues that the possibility should be entertained that this disease may be transmitted by ticks [as has previously been suggested by workers in the Netherlands East Indies].

In Ceylon, LUCAS (p. 886) has isolated a strain of *R. tsutsugamushi* [*R. orientalis*] from man by passage through guineapigs, white rats and white mice. He considers the white mouse to be the animal of choice for this work. VAN ROOYEN and DANSKIN (p. 463) note that two species of Egyptian gerbils, and the jerboa, are extremely susceptible to the rickettsia of scrub typhus.

SYVERTON and THOMAS (p. 879) describe a method of staining *Rickettsia tsutsugamushi*.

HICKS (p. 554) describes the post mortem findings in scrub typhus. The chief histological changes were proliferation of the reticulo-endothelial tissues and infiltration of interstitial tissues with mononuclear cells, especially in the heart, lungs and spleen. The naked-eye changes are described.

WILLIAMS *et al.* (p. 369) give a detailed account of the clinical features of scrub typhus, drawn from an experience of 626 cases. The original abstract should be consulted for details, but it may be mentioned that the value of the Weil-Felix reaction with *Proteus OXK* was confirmed, provided the strain of *Proteus* is suitable ; that an eschar was seen in only 59 per cent. of the cases ; that the death rate was profoundly influenced by lowered resistance due to hardship, malaria and dysentery ; and that there was no evidence of permanent cardiac disability in those who recovered.

LIPMAN *et al.* (p. 371) also describe the clinical features of scrub typhus, and the original abstract of this paper also should be consulted for details. They give a list of complications, in which cardiovascular disturbances are prominent. A similar description is given by BERRY *et al.* (p. 555), who regard the vascular changes found at post mortem to be of primary importance, myocardial and pulmonary lesions being secondary to them. They note that obstinate cardiac neurosis may occur if any suggestion of heart disease is made to the patient. LEVINE (p. 556) also stresses the fact that suggestion of heart disease may make an almost ineradicable impression on the minds of people suffering from scrub typhus, leading to neuro-circulatory asthenia. In actual fact, there were only two cases of true cardiac disease in 130 patients.

A comprehensive description of the clinical features of scrub typhus is given by MACHELLA and FORRESTER (p. 994).

In *Army Medical Department Bulletin* No. 41 (p. 112) there is a note on fluid retention in scrub typhus. This is a common feature of the disease, and is often relieved by diuresis which occurs relatively suddenly about the 14th day of disease ; this is associated with subjective improvement, and is usually followed by reduction of the fever.

A study of the blood chemistry in scrub typhus is reported by GOTTFRIED (p. 885) ; the details are numerous and should be sought in the original abstract.

WEDD (p. 111) reports an increase in " speckled lymphocytes " in the convalescent stages of scrub typhus, which is seen only rarely in other diseases. The cells are described, and it is noted that speckling occurs in a proportion of lymphocytes in normal blood.

LOGUE (p. 274) describes an outbreak of mite typhus among American troops on an island in the S.W. Pacific, and outlines the preventive measures which, when adopted, were successful. These comprised preparation and treatment of camping sites, rat control, the use of dimethyl phthalate and insecticidal powder. [In the abstract the word *kunal* is a misprint for *kunai* grass.]

In an outbreak of scrub typhus in the south Pacific, the incidence declined sharply after certain control measures were instituted :—trapping of rats, cutting and burning of *kunai* grass, spreading of sand, wearing of leggings, and the liberal use of repellents (MOREHEAD, p. 720). In the *Journal of the American Medical Association* (p. 799) is a note to the effect that the United States forces have substituted benzyl benzoate for dimethyl phthalate for the impregnation of clothing as a protection against mites.

In the prevention of scrub typhus among men engaged in clearing scrub, ZAIR (p. 111) notes that bulldozers are useful for this purpose, and that if manual clearing is necessary, the scrub should first be sprayed with kerosene and burned. Advice is given in regard to rat-control operations.

LEWTHWAITE (p. 980) refers to the immunity conferred by an attack of tsutsugamushi disease.

STEPHENSON (p. 553) reports a single case of fever of the typhus group, with a strong reaction to *Proteus OXK*, in the Sudan, where mite-borne typhus is not known.

Indeterminate type. Vector : tick.

MARIOTTE *et al.* (p. 721) report natural infection of *Rhipicephalus sanguineus* with rickettsiae of Rocky Mountain fever, in Mexico. BUSTAMANTE and VARELA (p. 203) have found Rocky Mountain spotted fever in rural areas of Mexico. The vector was probably *Rhipicephalus sanguineus.*

PLOTZ *et al.* (p. 636) have tested the sera of persons with Rocky Mountain spotted fever, by the Weil-Felix, complement fixation, rickettsia agglutination and mouse neutralizing tests, to find a satisfactory means of differentiating this disease from epidemic and murine typhus. The Weil-Felix results were irregular, as is usual in tick-borne typhus, and the rickettsia agglutination test did not afford good differentiation. The complement fixation reaction gave uniformly consistent results, with clear-cut differentiation. It was found that antibodies capable of neutralizing epidemic and murine toxins were present in Rocky Mountain spotted fever. [See also WOLSTENHOLME and GEAR, above.]

HARRELL *et al.* (p. 373) challenge statements which have been made to the effect that intravenous medication does more harm than good in Rocky Mountain spotted fever, and they claim that the collapse of the peripheral circulation which occurs corresponds to the condition of shock and may need treatment with plasma or blood. The administration of fluid should be very carefully controlled, as to amount and type—saline and glucose, or blood. The same authors (p. 888) think that in Rocky Mountain fever, as in burn shock, there is extensive leakage of proteins through the walls of blood vessels, into the tissues. They treat their patients, therefore, with transfusions of plasma, one effect of which is to promote the reabsorption of crystalloids into the vessels. This treatment is carefully controlled by estimation of non-protein nitrogen, serum proteins, and chlorides of the blood. A high-protein diet is useful.

The action of *p*-aminobenzoic acid in guineapigs infected with Rocky Mountain fever appears to be purely suppressive, but it prevented death in many of the animals, though all controls died (ANIGSTEIN and BADER, p. 888).

EDMUNDS (p. 464) has treated one patient, suffering from Rocky Mountain spotted fever, with penicillin. This was apparently very successful, but no value was found by FITZPATRICK (p. 996) in the treatment of experimental Rocky Mountain spotted fever with penicillin.

HEILIG and NAIDU (p. 30) refer to the fevers of the typhus group which have been seen in the State and City of Mysore, and to the complement-fixation tests carried out on some of these cases by TOPPING. The results of these tests

indicate that the disease is related to Rocky Mountain spotted fever rather than to other members of the typhus group. Cases of some fever of the typhus group, but without rash, are described from the United Provinces of India by BARDHAN (p. 29). PRADHAN (p. 29) describes cases of a typhus-like disease, possibly transmitted by ticks, which he has seen in recent years in Berar, India.

PESTANA (p. 638) gives reasons for his view that the typhus of São Paulo may not entirely be of the Rocky Mountain type, but may include cases of the flea-borne, murine, type.

PATIÑO-CAMARGO *et al.* (p. 799) proved that an adult *Ornithodorus parkeri* contained living rickettsiae 1,087 days after a feed on a guineapig with the spotted fever of Tobia. A related species, *O. rudis*, is a potential vector and is abundant in Tobia.

DE MAGALHÃES and ROCHA (p. 986) have produced inapparent infection in certain common Brazilian small animals, by injection of infective material from Brazilian exanthematic typhus. They describe the clinical types of this disease. [This form of typhus is presumably tick-borne.] The same authors (p. 988) have tried penicillin in Brazilian typhus [tick-borne] ; there seems to be some slight beneficial effect.

RODHAIN and BARLOVATZ (p. 887) discuss the histology of the eschar in the disease, found in the Belgian Congo, which resembles boutonneuse fever. An outbreak of tick typhus in East Africa is described by WALSH (p. 720), in which a local lesion was found in every case.

CAVAZZI (p. 113) has seen five cases of boutonneuse fever in the Ethiopian highlands.

KORSHUNOVA *et al.* (p. 274) give an account of tick typhus as it occurs in central Siberia. The infection is apparently found in ground squirrels and other rodents, and is transmitted to man by *Dermacentor nuttalli* and possibly by other ticks. A strain isolated from man immunized animals against Marseilles [? boutonneuse] fever. SHKORBATOV (p. 464) discusses tick-borne typhus in the far east of the Soviet Union, where the vector appears to be *Dermacentor sylvarum*. Serum reactions are most commonly given to *Proteus OX19*.

Bullis fever.

BADER and ANIGSTEIN (p. 639) report their experiments to determine the specificity of the rickettsiae isolated from *Amblyomma americanum* and from a patient with Bullis fever. The strains are not related to Q fever or Rocky Mountain spotted fever. The details of the experiments should be sought in the original abstract, but, in comment, MEGAW remarks that perhaps more than one short tick-borne fever may have been included under the name Bullis fever. BLAIR and BADER (p. 799) have induced fever in nine volunteers inoculated with material derived either from patients with Bullis fever or from infected ticks, and subsequently passaged through guineapigs. Many other attempts to infect man were unsuccessful. LIVESAY and POLLARD (p. 203) have carried out complement fixation tests on patients recovered from Bullis fever, using an antigen prepared from the spleens of infected mice ; most of the tests were positive. Control tests were negative. Sera from certain animals shot in the neighbourhood were also positive.

BRENNAN (p. 799) gives a list of ticks and vertebrates at Camp Bullis ; some of these may, perhaps, be important in relation to Bullis fever.

Trench fever.

In a discussion of trench fever, v. BORMANN (p. 462) states that abortive attacks are common, that shin-bone pains have little diagnostic value, and that less than one-third of the attacks in one outbreak were of the periodic

type. A pronounced leucocytosis with relative lymphocytosis is a feature of the febrile periods of trench fever, with a return towards normal during the afebrile intervals (BIELER, p. 204). HELD (p. 113) describes nodules, resembling rheumatic nodules, in the scalp and the skin of other parts of the body, which he believes to be the physical basis of the headaches, shin-bone pains, etc., of trench fever.

REUTER (p. 204) describes trench fever.

KIBLER (p. 639) notes that there may be difficulty in differentiating trench fever from influenza, paratyphoid, typhus and wound sepsis. The clinical features are very variable. He points out that the blood may be infective for a long time, and that it is therefore unsafe to use the patient as a blood donor for two years after the attack.

REUTER and SCHÄFER (p. 204) think that war nephritis and trench fever are variants of the same disease, largely because the periodicity and the pains are of the same type, and because nephritis often occurs in trench fever.

Solustibosan has been found useful in the treatment of trench fever (EBERLIN, p. 31). BEIGLBÖCK and LÖSCHER (p. 31) have treated trench fever with "Pyrifer", a colon bacillus vaccine, with some benefit. *Charles Wilcocks.*

MALARIA.

MACARTHUR, W. **A Brief Story of English Malaria.** *Post-Graduate Med. J.* 1946, July, v. 22, No. 249, 198–200.

SEZONISMO, Lisbon. Dez anos de luta contra a endemia. [**Ten Years of Antimalarial Work in Portugal.**] 159 pp. (Publicação da Direcção de Serviços Anti-Sezonáticos, 1942.)

——. A luta contra a endemia no ano de 1941. [**Antimalarial Work in 1941.**] 176 pp. (1942.)

——. A luta contra a endemia no ano de 1942. [**Antimalarial Work in 1942.**] 230 pp. (1943.)

——. Trabalhos originais-1942. [**Original Papers, 1942.**] 212 pp. (1943.)

——. A luta contra a endemia no ano de 1943. [**Antimalarial Work in 1943.**] 239 pp. (1944.)

——. Trabalhos originais-1943. [**Original Papers, 1943.**] 90 pp. (1944.)

This publication is issued each year by the Ministry of the Interior, Public Health Department, Lisbon, and is a record of the antimalarial activities of the previous year. The word Sezonismo was used for malaria by Ricardo JORGE, who, though not the originator of the Portuguese antimalaria organization, was well known for his work on the subject.

The first number of *Sezonismo*, issued in 1942, contains an account of 10 years of this work up to 1940. The later numbers cover the years 1941, 1942, and 1943, separately. Those who wish to follow the malaria investigations in Portugal should consult these publications.

In addition to this general account of routine work, a separate publication with the same name is issued each year, and contains original papers of work done in the previous year. *Charles Wilcocks.*

PAPAFIGOU, Théodora. Deux cas d'infection à *Pl. ovale* Stephens en Grèce. [**Two Cases of Infection with *P. ovale* in Greece.**] *Rev. Paludisme et Méd. Trop.* 1946, June 15, v. 4, No. 27, 180–83, 10 figs. [12 refs.]

CORRÊA, R. R. Sôbre a incidência da malaria, em especial do *Plasmodium malariae* (Laveran, 1881), no Ramal de Itapura. [**The Incidence of Malaria, especially *P. malariae*, in the Ramal de Itapura, Brazil.**] *Arquivos de Hig. e Saude Pública.* 1945, Dec., v. 10, No. 26, 181–7, 3 figs. on 1 pl. & 1 map. [17 refs.] English summary.

CODA, D. Malária quartã no litoral sul. [**Quartan Malaria in Iguape, São Paulo State, Brazil.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1945, Sept., v. 10, No. 25, 79–80. English summary (3 lines).

MARTINS, A. V. & VERSIANI, V. Novo foco de malaria quartã no estado de Minas Gerais. [**A New Focus of Quartan Malaria in Minas Geraes.**] *Brasil-Medico.* 1946, May 4 & 11, v. 60, Nos. 18/19, 168–9.

RIBBANDS, C. R. **Effects of Bush Clearance on Flighting of West African Anophelines.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 33–41, 2 figs.

The experiments described in this paper were conducted in an attempt to discover if the eradication of low vegetation around human dwellings reduced the numbers of anopheline mosquitoes attracted to them.

The main work was done at a village near Sekondi, Gold Coast, between January and March 1942. In this village all but three of the huts were pulled down; the observer used one of them, and seven Africans were installed in the other two. There was a large swamp 880 yards to the east. To allow for any differences in individual attraction to mosquitoes, the Africans were regularly changed about. Daily catches of mosquitoes were made in the two huts between 7 a.m. and 9 a.m., and night catches were made in one of them. These, the "experimental catches", were compared with simultaneous "control catches" made in three other huts; one, the "inner control" hut, 190 yards away, was newly erected for the experiment in the direction of the swamp and was occupied by three Africans. The other two, the "outer control" huts, were already established in a south easterly direction; one at 650 yards distance, occupied by three Africans and one at 880 yards, occupied by one African; the catches in these two huts were averaged. After three weeks the bush was cleared around the two experimental huts for an average radius of 140 yards; this work took five days. Catching continued during this time and for another three weeks.

Counts of anopheline mosquitoes caught in the experimental huts were calculated as percentages of the corresponding counts in the control huts. These figures are presented, graphically and in tables, in three groups—before, during, and after the bush clearance. They show little difference between the proportion of female *A. funestus* and *A. gambiae* caught in the experimental huts after the clearance, and the proportion which reached the huts before the clearance; males entered in the same proportion as before. During the clearing operations the proportion of females dropped to nearly a quarter and of the males to one-half of that before the clearance; this reduction is attributed to the masking of the scent of man by the odour of the cut decaying vegetation.

A somewhat similar experiment had already been made during August and September 1941 at Aberdeen, near Freetown, Sierra Leone, where the predominant anopheline was *A. melas*. Catches were made for 14 nights in seven huts, six of them in a clearing and the seventh 25 yards from the others but ten yards inside the bush, which reached 15 ft. in height; the African occupants

changed huts in rotation. Catches made in the bush hut were compared with those made in the nearest hut in the clearing, and though there were variations on different nights, the bush hut provided an average nightly yield, for the 14-day period, of 47·4 per cent. of the total catch.

There are features about these experiments which may appear to be unsatisfactory to the reader, such as the number of Africans, number, size and age of huts, but the author believes that the results indicate that bush clearing around dwelling places is not justified as a measure for reducing anopheline infestation, a conclusion which is meant to apply only to *A. gambiae* and *A. funestus* in West Africa. *H. S. Leeson.*

VARGAS, L. Consideraciones sobre el complejo del *Anopheles pseudopunctipennis*. [**Studies on the** *A. pseudopunctipennis* **Complex.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 265–70, 1 fig. [15 refs.] English summary.

"The *Anopheles pseudopunctipennis* complex, studied up to now discloses the following subspecies: *typicus* Theobald, 1901; *franciscanus* McCracken, 1904; *boydi* Vargas, 1939; and *willardi* Vargas, 1941. The author mentions the most remarkable morphological data useful in the identification of these. The subspecies *typicus* acquires importance in the transmission of malaria only when the high numbers of individuals form a large population."

CORRÊA, R. R. Da infecção natural, pela plasmodiose malárica, do *Anopheles* (*Kerteszia*) *cruzi* D.-K., 1908. [**Natural Infestation with Malaria of** *A. cruzi*.] *Folia Clin. et Biol.* São Paulo. 1943, v. 15, No. 1, 23–32, 11 figs. [11 refs.] English summary.

FONSECA, J. A. B. & UNTI, O. Infecção experimental de anofelinos de regiões indenes à malária. [**Experimental Malarial Infection of Anophelines from Areas of Endemic Malaria.**] *Folia Clin. et Biol.* São Paulo. 1943, v. 15, No. 1, 43–52.

BRIGGS, G. D. S. **A Case of Cerebral Malaria on Board a Troopship** [Memoranda.]. *Brit. Med. J.* 1946, July 13, 51–2.

MARSHALL, E. K., Jr. **Chemotherapy of Malaria, 1941-45**. *Federation Proc.* Baltimore. 1946, June, v. 5, No. 2, 298–304. [15 refs.]

ENGLISH, J. P., CLARK, J. H., SHEPHERD, R. G., MARSON, H. W., KRAPCHO, J. & ROBLIN, R. O., Jr. **Studies in Chemotherapy. XIV. Antimalarials. The Synthesis of Substituted Metanilamides and Related Compounds.** *J. Amer. Chem. Soc.* 1946, June, v. 68, No. 6, 1039–49, 4 figs. [Refs. in footnotes.]

ANN. TROP. MED. & PARASIT. 1946, Apr., v. 40, No. 1, 80–87, 7 figs. on 2 pls. **The Effects of Mepacrine on the Gastro-Intestinal Tract of Man.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G. *et al.*) & Nuffield Institute for Medical Research, Oxford (FRANKLIN, K. J. *et al.*).]

Mepacrine was given to numerous volunteers in various doses, and one and a half hours later they were given a barium meal so that the movements of the alimentary canal could be observed radiologically. Twelve women received single doses of 0·6–1·0 gm. mepacrine. Clinically they experienced headache, often severe, nausea, sometimes repeated vomiting, colicky abdominal pain and diarrhoea. In more severe cases, fever and prostration occurred. These symptoms began to disappear after 8–9 hours. Radiologically, immediately

after the taking of the barium meal there was gastric hypersecretion, hyperperistalsis, increase of tone of the pyloric antrum followed by atony, and pylorospasm. Emptying of the stomach was delayed. The intestines were abnormally active and the rate of passage of the meal along them was increased, although there was delay at the ileo-caecal valve. Once the meal entered the colon, it advanced very rapidly ; there was also marked outpouring of secretion in the colon. The gall bladder appeared normal, and no significant change could be detected in the flora of the faeces.

On the other hand, a large number of volunteers on a suppressive régime of 0·1 gm. mepacrine daily rarely showed gastro-intestinal disturbances, and such disturbances as did occur were slight or unimportant. Fractional gastric analyses were carried out on the second day of taking 0·1 gm. mepacrine, but they revealed no significant abnormality. In 12 volunteers gastroscopy was performed. The gastric mucosa as a whole was normal, but immediately around the site of the tablet there was hyperaemia, and the accumulation of thick mucus ; but this effect was too slight to explain the symptoms which are sometimes experienced. Two patients with quiescent chronic ulcerative colitis received 0·1 gm. mepacrine daily for a fortnight ; there was no change in their general condition or in the bacterial flora of the stools.

It is recalled that widespread disturbances, especially vomiting and diarrhoea, occurred among the troops in North Africa in 1943 when they were given 0·2 gm. mepacrine twice weekly. The symptoms occurred most frequently after the third dose, developing 3–10 hours after the dose had been taken. Investigations at the time had shown that they were not psychogenic, they were not due to abnormally toxic batches of mepacrine and they were not due to some bacterial infection. In the present investigation eight volunteers were given 0·2 gm. twice weekly. Six volunteers showed no ill-effects ; two volunteers experienced severe symptoms after the third dose, resembling those seen in North Africa. The concentration of mepacrine in the plasma of these two volunteers was within normal limits. It is concluded that when a dose of mepacrine is repeated at intervals greater than two days, the tolerance for mepacrine in some of the subjects may be reduced by the time the third dose is given, and that such a régime should never be used. *F. Hawking.*

MANDEKOS, A. G. [**D.D.T. (Neocid, Gesarol, Gix). A New Insecticide which will revolutionize the Methods of controlling various Diseases transmitted by Insects.**] *Hellen. iatr.* Salonica. 1945, repr. 16 pp. [In Greek. English summary.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, June, v. 34, Pt. 6, 99.]

From laboratory and field experiments carried out in Greece in 1943 and 1944, it is concluded that Neocide (5 per cent. DDT in talc) is effective against larvae and adults, but not eggs or pupae, of *Anopheles* and *Culex*. Contact with the powder or with a suspension of 1–6 gm. Neocide in 1,000 cc. water with the addition of 2 cc. kerosene caused adults and larvae to die in 3–4 hours. Ceilings and walls of bedrooms or stables can be kept free from mosquitos for at least five weeks by the application of 1 gm. Neocide in 2 cc. kerosene and 18 cc. water per sq. metre [4·65 mg. DDT per sq. ft.]. A suspension of 2 gm. Neocide and 2 cc. kerosene in 1,000 cc. water applied at 70 cc. (7 mg. DDT) per sq. metre [about 1 oz. DDT per acre] to breeding places of races of *Anopheles maculipennis*, Mg., including var. *sacharovi*, Favr. (*elutus*, Edw.), gives very good initial kill, but an application must be made every week. In the fast-flowing streams in which larvae of *A. superpictus*, Grassi, occur, better results are obtained if a larger quantity of Neocide is used (160 cc. of a suspension containing 5 gm. Neocide and 10 cc. kerosene per 1,000 cc. water). In 1944,

this dosage was used in breeding places in Salonica, and the total number of Anophelines taken in ten catching stations in the city and its outskirts was 85, compared with an average of 89·1 and a range from year to year of 38·8 to 166·5 in 1939–43, when Paris green was applied by a dustless method. Comparative figures are given showing the amounts of DDT required per unit area for spraying walls or treating breeding places by the methods of application described by the author and by Smith.

BRUMPT, E. Grande utilité de deux plasmodies aviaires : *Plasmodium gallinaceum* Brumpt 1935 et *Plasmodium lophurae* Coggeshall, 1938, pour l'étude scientifique et pratique du paludisme humain. [**The Great Value of** *P. gallinaceum* **and** *P. lophurae* **for the study of Human Malaria.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 199–203.

TRYPANOSOMIASIS.

STEWART, J. L. **Eradication of** *Glossina* **in the Naboggo Valley, Gold Coast.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 99–103.

Animal trypanosomiasis made it impossible to keep any cattle, except the relatively resistant and inferior local dwarf breed, in the Naboggo valley. The tsetse present consisted of *Glossina palpalis* and *G. tachinoides*. The fly appeared dependent on the bush fringing the river, a meandering stream which is converted into separate pools in the dry season (November to June). The fringing bush in this whole valley was cleared selectively. Experiment showed that only the trees fringing the water need be removed ; these were cut at the beginning of the dry season, and the stumps completely burned in May. This needed supervision, but with care gave excellent results ; maintenance of the clearing proved practicable.

Erosion after clearing was feared, but the river never flows rapidly, and the quick and profuse growth of grass in cleared areas held the soil together. Some damming was done to conserve water for domestic use and for irrigation, as well as to prevent erosion.

The economic value of the work was soon manifest. The valley was able to maintain a much larger population of cattle of superior breeds (susceptible to trypanosomiasis). *Kenneth Mellanby.*

TRYPANOSOMIASIS COMMITTEE OF SOUTHERN RHODESIA. **The Scientific Basis of the Control of** *Glossina morsitans* **by Game Destruction.** *Rhod. Agric. J.* v. 42, No. 2, 124–8 ; also as *Bull. Minist. Agric.* [*S. Rhod.*] No. 1303, 6 pp. Salisbury, S. Rhod. 1945. [Summary taken from *Rev. Applied Entom.* Ser. B. 1946, June, v. 34, Pt. 6, 103–4.]

Measures have been taken in Southern Rhodesia during the past 25 years to create and maintain game-free zones in order to prevent the extension and ultimately cause the retrogression of *Glossina morsitans*, Westw. The regular hosts of *G. morsitans* are the larger grazing and browsing mammals available all the year round, and it also has occasional hosts, which are nocturnal, exceptionally active, migratory or seasonally hidden by long grass. It must obtain meals at regular intervals to replace water lost by evaporation. The extermination of most of its usual hosts deprives it of opportunities of obtaining regular meals and forces it to expend energy seeking other sources of food and thus lose much moisture, so that the death rate rises far above normal and

females may abort. To eliminate *G. morsitans* from an area, therefore, it is not necessary to exterminate every species of animal on which it can feed ; it is sufficient to eliminate those that provide a dependable source of food throughout the year. When this has been done, the fly cannot support life when grass is high and dense. As *G. pallidipes*, Aust., can find its prey even in thick vegetation, game destruction has to be very drastic to be successful by itself in eliminating this species. If a zone that has been freed of *G. morsitans* has its ends in fly-free country or is 50 miles or more long, game can be allowed to re-enter it by moving the shooting zone forward into the fly belt without increasing its width (10–20 miles). The desirability of doing this is discussed. It is pointed out that the presence of much game in a cattle area results in loss of pasturage and increases the difficulty of controlling tick-borne and other diseases of stock, and that certain species destroy crops or are a menace to human life.

RODHAIN, A. J. Documents pour servir à l'histoire de la maladie du sommeil au Congo belge. (Deuxième note.) La trypanosomiase humaine dans le district de l'Aruwimi en 1907 et en 1908. [**Documents relating to the History of Sleeping Sickness in the Belgian Congo. 2. Human Trypanosomiasis in Aruwimi District, 1907-08.**] *Inst. Roy. Colonial Belge—Bull. des Séances.* 1946, v. 17, No. 1, 368–79, 1 folding map.

FLOCH, H. & DE LAJUDIE, P. Recherches sur la trypanosomiase humaine américaine en Guyane française. *Rhodnius prolixus* et *Rhodnius pictipes* vecteurs naturels de choix de *S. cruzi*. [**Study of** *Trypanosoma cruzi* **Infection in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 117.* 1945, Nov., 5 pp.

Triatomidae captured in French Guiana belong to one or other of the following species : *Rhodnius prolixus, R. pictipes, Triatoma rubrofasciata, Panstrongylus geniculatus* and *Eratyrus mucronatus*. LAROUSSE has recorded *R. robustus* also, but the authors have not met with it. They have found trypanosome infection in *T. rubrofasciata, R. prolixus* and *R. pictipes*, but in the case of the first they could not obtain the blood forms, and animal inoculations in the laboratory remained negative and on one occasion only was xenodiagnosis positive. They think, therefore, that the trypanosome present in this insect is more often that common in bats, not the human type of *T. cruzi*. Of four specimens of *R. pictipes*, three were infected ; this has not before been noted as infected in nature. Further examination has shown that of 72 *R. pictipes* examined 65 were positive ; of *R. prolixus* 68 out of 80, but only 29 out of 91 *T. rubrofasciata*. The two former are, therefore, to be regarded as the natural vectors in French Guiana, *T. rubrofasciata* less commonly. The authors conclude : " The experimental xenodiagnostic test seems to us to be of much value in determining what are the natural vectors of choice of *S. cruzi* in any given district." *H. Harold Scott.*

BRASIL, A. Forma cardíaca crônica da Doença de Chagas. [**Chronic Cardiac Lesions in Chagas's Disease.**] *Hospital.* Rio de Janeiro. 1946, Feb., v. 29, No. 2, 199–224, 23 figs. [17 refs.] English summary.

In August 1941, a Congress lasting for a week was held in Belo Horizonte in honour of Carlos Chagas. This is one of the papers read at that Congress. It is a concise but comprehensive account of the cardiac complications of this disease, dealing with the symptoms, diagnosis, prognosis and treatment, and illustrated by 89 electrocardiographic tracings. Diagnosis is stressed between

this and arterio-sclerosis, syphilis, rheumatic carditis, diphtheria, congenital heart disease, among other conditions. The whole is a very readable summary but there is nothing fresh and it does not lend itself to abstract. Those wishing to renew their knowledge of the subject would do well to read the English summary, which is fairly full and contains all the important points of the original. *H. Harold Scott.*

RAMOS, J., Jr. & LAUS F., J. A. Miocardite crônica na tripanosomíase americana. Considerações clinicas em tôrno de seis casos. [**Chronic Myocarditis in American Trypanosomiasis. Discussion of Six Cases.**] *Hospital.* Rio de Janeiro. 1946, Feb., v. 29, No. 2, 231–50, 14 figs. English summary.

Evidence has been accumulating in recent years to show that sufferers from non-valvular disease of the heart often owe their condition to *T. cruzi* infection. The present communication deals with six patients, 5 men and 1 woman, their ages ranging from 29 to 66 years. The dates of infection could not be determined in four ; in the other two it was 10 and 15 years previously, but all had lived in *Triatoma*-infested localities. Their symptoms were mainly dyspnoea and epigastric pain on exertion, and marked debility with palpitation and headache, giddiness and cough with mucoid sputum. None of these symptoms is, of course, characteristic of Chagas's disease ; they are common to myocarditis of any origin, but electrocardiograms show that the lesion is, in this disease, situated in the Bundle of His or in the sinoauricular node [we must remember that the conclusions are here based on a very small number of cases], with resultant arrhythmia and signs of heart-block. Of the six cases detailed, three ended fatally with the usual signs of cardiac failure. The others improved, in that oedema cleared up, the dyspnoea became less troublesome and the heart diminished in size. These three were diagnosed, one by a positive xenodiagnostic test, the other two by positive Guerreiro-Machado reactions. The three fatal cases had given negative results to xenodiagnosis, but the Guerreiro-Machado test could not be carried out owing to temporary lack of antigen ; diagnosis in them was made by post-mortem findings. The moral to be drawn from this is that *T. cruzi* infection should be suspected and looked for in all patients with myocardial lesions who live in, or have come from, regions where the vectors prevail. *H. Harold Scott.*

MAZZA, S., BASSO, G. & BASSO, R. Investigaciones sobre enfermedad de Chagas. Esquizotripánides ulcerosas tardías en enfermedad de Chagas y otras manifestaciones eruptivas. [**Studies in Chagas's Disease. Late Ulceration and other Cutaneous Manifestations.**] *Universidad Buenos Aires : Misión de Estudios de Patologia Regional Argentina (Jujuy), Publicacion No. 71.* 1946, 42 pp., 32 figs.

Several eruptions may be seen in patients infected by *T. cruzi* ; urticarial, erythemas, morbilliform rashes have been described, but the present article illustrates other forms, perhaps rarer, certainly more distinct. Small, punched-out ulcers may be seen on the foot, lip and elsewhere. A good illustration shows the differences between these and the punched-out ulcer of American leishmaniasis. Crusted healing ulcers of the lips and face, and papular eruptions of the face and neck, are not uncommon ; another photograph shows a dense papular eruption of the thigh ; yet another, a child with extensive impetigo-like lesions of the chin, neck and chest. These lesions usually heal well under treatment with 7602 (Ac) Bayer, but leave pigmented scars.

H. Harold Scott.

DE FREITAS, J. L. P. Inquérito preliminar sôbre moléstia de Chagas no Município de Cajurú, Estado de São Paulo, Brasil. [**Preliminary Investigation of Chagas's Disease in Cajarú, Brazil.**] *Hospital.* Rio de Janeiro. 1946, Feb., v. 29, No. 2, 155–65. [10 refs.] English summary.

FEVERS OF THE TYPHUS GROUP.

TOPPING, N. H. & SHEPARD, C. C. **The Preparation of Antigens from Yolk Sacs infected with Rickettsiae.** *Pub. Health Rep.* Wash. 1946, May 17, v. 61, No. 20, 701–7, 1 fig. [11 refs.]

Three methods of preparing antigen from yolk sacs infected with *Rickettsia prowazeki*, *R. mooseri*, *R. rickettsi*, *R. burneti*, and *R. orientalis* are described. It was found that no single method was satisfactory for all these species of rickettsiae. All the methods were modifications of Craigie's diethyl-ether method. The antigenic potency of the products was estimated by complement-fixation tests applied to the sera of guineapigs which had been immunized by homologous strains of rickettsiae. In all three methods homogenized yolk-sac cultures were used. In Method 1, a 10 per cent. suspension was shaken directly with one-and-a-half volumes of ether ; in Method 2, a 10 per cent. suspension was centrifuged to sediment the rickettsiae before treatment with ether, and the rickettsiae were resuspended in one-tenth of the original volume of saline, so there was a ten-fold concentration. In both of these methods, when *R. prowazeki* and *R. mooseri* were dealt with, the final product contained large quantities of antigen released by the ether and contained in the supernatant fluid after centrifugation. With *R. rickettsi* much less of this soluble antigen was released, with *R. burneti* and *R. orientalis* there was no release at all, but rather a loss of antigen. The methods, therefore, were quite unsuitable for the preparation of *R. orientalis* antigen.

In Method 3 the homogenized yolk sacs were shaken with 10 volumes of ether at a temperature of 4°C. for 30–60 minutes. After standing for a short time the ether became yellow, and a " reddish mass of tissue " fell to the bottom. The ether was decanted and fresh ether was added once or twice till it ceased to become yellow. After final decanting, about 1·0 cc. of distilled water was added for each gramme of yolk sac and, after shaking, the ether still in solution was removed under a partial vacuum. The suspension was kept overnight in a refrigerator and then centrifuged. The antigens were contained in the clear-red supernatant ; in the case of *R. orientalis* the sediment also contained a considerable amount of antigen. By this method a satisfactory antigen was obtained from yolk sacs infected with *R. orientalis* ; the complement-fixation titre was 1–128 as compared with one of 1–8 for the original crude 10 per cent. suspension and titres of 1–2 for the preparations made by Methods 1 and 2. With *R. burneti* there was actually a loss of antigen when Method 3, or any other method of ether extraction, was used. With *R. rickettsi*, *R. prowazeki*, and *R. mooseri*, Method 3 gave much the same results as the other two methods ; the titre with *R. rickettsi* was 1–32, with the other two organisms it was in excess of 1–2,048.

The authors state quite clearly that no demonstrable immunization has been produced in mice inoculated subcutaneously with any antigens prepared from yolk sacs infected with tsutsugamushi disease. *John W. D. Megaw.*

TOPPING, N. H. & SHEPARD, C. C. **A Method for the Preparation of Tsutsugamushi (Scrub Typhus) Antigen from Infected Yolk Sacs.** *Pub. Health Rep.* Wash. 1946, May 31, v. 61, No. 22, 778–81.

This paper, by the same authors as the one reviewed above, was scheduled for publication on March 2, 1945, but was withheld because of the subject matter. The method described has presumably been superseded by Method 3 dealt with in the preceding abstract, but the paper will be of historical interest to all workers on the preparation of rickettsial vaccines.

John W. D. Megaw.

CHALKE, H. D. **Typhus: Experiences in the Central Mediterranean Force.** *Brit. Med. J.* 1946, June 29, 977–80; July 6, 5–8, 1 chart & 1 fig.

The author tells how the allied forces succeeded in keeping remarkably free from typhus fever during military operations in North Africa, Italy, and Yugoslavia, in spite of the great prevalence of the disease among the people of these countries, and in spite of the fact that none of the hygiene staff officers were informed of the projected landing in North Africa till the forces had actually embarked.

The preparations for dealing with the disease among the British troops consisted in the provision of large quantities of the powder A.L.63 (which contained derris and naphthalene) and of large numbers of portable disinfectors; medical-staff-officers were inoculated with a Cox-type vaccine; and talks were given before landing to officers and men.

After landing, contact was made with the French Chief Officer of Public Health of Algeria, who stated that between October 1941, and September 1942, nearly 40,000 cases of typhus fever had been reported, and that he believed the real incidence to have been at least six times as high as this. One important safeguard was the fact that hardly any cases occurred in the large towns, in which the people had been vaccinated by Blanc's liver murine vaccine. About two million persons had received this vaccine by the end of 1942. The killed vaccine of Durand and Giroud was used for doctors and others exposed to special risks, and although there were many cases of typhus among the 71,000 persons who received the vaccine, no deaths were known to have occurred. All the American troops had been vaccinated before landing, but for the first few months the British troops were not protected in this way, and they had to rely on regular hand-dusting with A.L.63 and on intensive propaganda. In 1943 there were about 34 cases of louse-borne typhus and six of other forms of typhus among the British forces. When native-labour forces were enlisted, the recruits were bathed, disinfested, and inoculated with the Blanc vaccine.

The author tells the story of the much publicized epidemic in Naples. The city was occupied by the Fifth Army in October 1943; in November there were rumours that typhus was occurring, and on investigation it appeared that the reports were well-founded. A conference of British and American hygiene officers was at once called; this was attended by Italian public-health doctors. A representative committee was set up, a meeting of the medical men of Naples was held, and prompt action was taken to search for cases and to disinfest all hospital patients and contacts.

From November 16 the incidence in successive weeks was:—18, 18, 22, 45 and 36 cases; then a sudden rise occurred in the week December 22 to 28, with 138 cases.

Early in December Dr. Soper and Dr. Davis of the Rockefeller Foundation arrived, and by the middle of the month systematic case-searching and widespread disinfestation of contacts with the American powder MYL (containing

pyrethrum) were in operation. An important point was the initiation of the system of disinfestation by applying the powder with dust guns without removing the clothing; by this method large numbers of persons could be disinfested; as many as 60,000 were dealt with daily, and by the end of February 1944, 2,250,000 dustings had been carried out.

The U.S.A. Typhus Commission team arrived in December and began work early in January 1944. Details of the very thorough system of control established under the direction of the Commission have already been fully reported; the operations were unprecedented, both in their magnitude and in the completeness of the organization. Large quantities of 10 per cent. DDT powder became available early in January.

The author states that the measures adopted up to December 23 had already brought the epidemic under control, because after the week ending January 11 there was a sudden fall from 340 to about 170 in the weekly number of cases reported; he assumes a time lag of about 18 days, made up of the 12-day average incubation period and the average delay of six days in reporting the cases. [This view will not be universally accepted; there were still as many as 130 cases in the week ending February 8, and in the following week there was a sharp drop to 40 cases, so that allowing for the same time lag it may be argued that control became really effective towards the end of January.]

The conditions prevailing in Naples at the time of the epidemic are described in vivid language; they were such that a devastating epidemic would have been expected to occur during the first half of 1944, whereas the disease had disappeared from the city by the middle of April.

The remarkable results obtained are attributed to the perfection of the methods adopted and to the close and amicable co-operation between the British and American medical officers, the U.S.A. Typhus Commission, the Rockefeller Foundation team, the Allied Commission, the Allied Military Government, the Italian civil and military doctors, and the troops themselves.

The British troops and their attached civilian workers were protected only by MYL or A.L.63 powder, few of them were inoculated, yet only two or three cases occurred in this large group. The only British soldier attacked was a deserter who was heavily infested with lice. *John W. D. Megaw.*

ZARAFONETIS, C. J. D., ECKE, R. S., YEOMANS, A., MURRAY, E. S. & SNYDER, J. C. **Serologic Studies in Typhus-Vaccinated Individuals. III. Weil-Felix and Complement-Fixation Findings in Epidemic Typhus Fever occurring in the Vaccinated.** *J. Immunology.* 1946, May, v. 53, No. 1, 15–30. [17 refs.]

The authors, working with the U.S.A. Typhus Commission in Cairo, have studied the Weil-Felix and complement-fixation reactions occurring at various stages of attacks of typhus fever in patients who had been protected by an epidemic-typhus vaccine of the Cox type. Of the 31 cases investigated, 29 were diagnosed with certainty, or with a high degree of probability, as epidemic typhus, the other two were cases of murine typhus contracted in West Africa. The conclusion was reached that the reactions can safely be used to establish a laboratory diagnosis of typhus fever in vaccinated persons, provided that allowance is made for the higher degree of cross-fixation for epidemic and murine typhus that occurs among these persons as compared with unvaccinated patients. The paper is complementary to one by PLOTZ and WERTMAN, who carried out similar tests on murine-typhus patients previously vaccinated with epidemic-typhus vaccine [see this *Bulletin*, 1946, v. 43, 429].

In all the 31 patients the rises observed in the titres of the Weil-Felix (*OX19*) and complement-fixation reactions were higher than had ever been observed by the authors among healthy persons who had received "booster" doses of

the vaccine, or among vaccinated persons who were suffering from other febrile diseases. In two of the 29 cases of epidemic typhus, the murine-complement-fixation titre reached the same high level as the epidemic titre, but in most of the other cases the epidemic titre was four or more times as high as the murine.

Strangely enough, the two patients diagnosed as having murine typhus had epidemic titres rising to 1–512 and 1–1,024, whereas their murine titre was only 1–256 in each case.

The authors suggest that the high degree of cross-fixation observed among vaccinated patients may be due to the presence of a "common antibody" produced in the serum, in response to the action of the antigen common to epidemic and murine rickettsiae that is contained in the vaccine; the common antibody would be expected to fix complement in the presence of antigens either of the epidemic or murine type.

Two of the patients suffered from laboratory infections; the serum of one of these had given an epidemic-typhus complement-fixation reaction at a titre of 1–8 about two months before the onset, and also on the second, third, and fourth days of the illness; the titre rose to 1–32 on the fifth day; this patient's serum was known to have contained a considerable amount of neutralizing antibodies two months before the illness, as shown by tests with gerbils, so that the immunity known to exist beforehand had obviously not been enough to prevent infection, but only to modify the severity of the attack.

John W. D. Megaw.

SHEPARD, C. C. & WYCKOFF, R. W. G. **The Nature of the Soluble Antigen from Typhus Rickettsiae.** *Pub. Health Rep.* Wash. 1946, May 31, v. 61, No. 22, 761–7, 8 figs. on 4 pls.

With the help of the electron microscope the authors have investigated the physical characteristics of the filter-passing "soluble antigen" which is liberated from suspensions of epidemic and murine rickettsiae by ether treatment. This antigen has now been shown to consist of "sub-microscopic particles of a capsular substance" which adheres to and partly envelops the rickettsiae contained in a suspension purified by centrifugation. The term "droplets" is also applied to the particles, which, though not uniform in size, are so small that most of them could pass through bacterial filters. A photograph, at a magnification of 18,000 diameters, shows clearly a large number of the rounded particles, present in a film prepared by evaporating a minute drop of the supernatant fluid obtained by high-speed centrifugation of warm-ether extracts of homogenized yolk sacs infected with murine rickettsiae. The dried films were "shadowed" by coating them with an obliquely deposited film of gold by the method of WILLIAMS and WYCKOFF (*J. of Applied Physics*, 1946, v. 17, 23).

Seven other photographs prepared on the same lines, show: (1) *R. prowazeki* and *R. mooseri* from untreated suspensions; (2) *R. prowazeki* after extraction with ether, and demonstrating that the liberation of the particles from the capsular substance is much more active and complete with warm-ether treatment than with cold-ether treatment; and (3) clumps of particles of soluble murine antigen agglutinated by homologous immune serum of rabbits.

John W. D. Megaw.

GIROUD, P. Démonstration faite au sujet des corps homogènes, inclusions du typhus exanthématique. [**Demonstration of the Homogeneous Inclusion Bodies of Exanthematic Typhus.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 83–6.

The author describes the results of further investigation into the various forms assumed by the rickettsiae of typhus fever and the products of their action on the invaded cells.

The bodies now described were obtained from animals whose initial resistance to infection was being broken down. Smears containing the bodies were fixed, treated with acetone, and stained by Giemsa's method.

Side by side with blue-staining homogeneous bodies, other intracellular, purple ("aubergine-coloured") rounded bodies of similar size were seen; on the surface of the latter there were one or more small masses of about one μ in diameter, which gradually became transparent, lost their central portion, and assumed the form of rings with one or more thickenings. At a later stage each ring broke into two or three parts, each of which at first consisted of a slightly curved rickettsia with pointed ends, and later became like a normal bacilliform rickettsia.

Another transformation of blue-stained homogeneous bodies was sometimes seen in which they became broken up into transparent elements of three to four μ in diameter, each containing an unstained vacuole which later showed a chromatin-stained particle in its centre. Sometimes each element contained three or four vacuoles of the same kind. Soon the appearance of the original homogeneous body became changed to one of an enlarging granular body resembling a compact swarm of bees.

The author regards the homogeneous bodies as analogous with bacterial spores and as being capable of giving rise to bacilliform rickettsiae in the ways described.

[For the earlier studies on this subject by the author and PANTHIER, see this *Bulletin*, 1943, v. 40, 764; and 1942, v. 39, 753.] *John W. D. Megaw.*

CRAIGIE, J., WATSON, D. W., CLARK, Eina M. & MALCOMSON, M. Elizabeth. **The Serological Relationships of the Rickettsiae of Epidemic and Murine Typhus.** *Canadian J. Res.* Sect. E. Med. Sci. 1946, Apr., v. 24, No. 2, 84–103, 5 figs. [17 refs.]

This paper was submitted as a confidential document in September 1943. Breinl and Madrid strains of epidemic rickettsiae and the Castañeda strain of murine rickettsia were used in the experiments, which are described in detail by the authors.

Specific differences were shown to exist between the complement-fixing antibodies of epidemic and murine rickettsiae by removing the antibody common to both types from immune sera by the addition of rickettsiae of the heterologous types. Sera treated in this way were tested by the complement-fixation reaction and gave much higher titres with the homologous than with the heterologous antigen.

The type-specific complement-fixing antigen was found to be inactivated by heating for one hour at a temperature between 56° and 65°C. and so was shown to be thermolabile; the thermostable antigen remaining after this treatment was found to be the same for both types of rickettsiae.

The Giroud rabbit-skin reaction was found capable of being applied to differentiate between the specific heat-labile antigens of epidemic and murine rickettsiae.

Small doses of murine or epidemic vaccines immunized mice against the toxic factors of homologous, but not of heterologous, rickettsiae: when these vaccines were heated to 56°C. for 45 minutes much larger doses were needed to immunize the mice, and the resulting immunity was the same for heterologous as for homologous toxins.

From the above and other experiments it appeared that epidemic and murine rickettsiae contained a common thermostable antigen and that each of the two types of rickettsiae contained a type-specific thermolabile antigen.

The authors state that there seems to be full justification for the suggestion made by Felix that there is an analogy between the heat-labile and heat-stable antigens of rickettsiae on the one hand, and the Vi and O antigens of the typhoid bacillus on the other.

No claim is made that the findings described necessarily apply to every strain of the two types of rickettsiae; the authors refer to the need for an "antigenic analysis of intermediate strains."

Full details of these important experiments will be found in the paper.

John W. D. Megaw.

JOHNSON, Mary B. & DAMON, S. R. **The Serologic Diagnosis of Endemic Typhus. III. The Incidence and Titer of Complement-Fixing Antibodies in Random Samples of the Population in Endemic and Nonendemic Typhus Areas.** *J. Lab. & Clin. Med.* 1946, May, v. 31, No. 5, 550–51.

Complement-fixation tests were carried out for endemic typhus [presumably the murine type] on the sera of :—(*a*) 500 persons who formed a random sample of the population of Houston County in southern Alabama, where the disease is endemic; and (*b*) 400 corresponding persons from Morgan County in northern Alabama, where the disease is rare.

In the former group there were 58 reactions at titres of 1–4 or over; in the latter there was only one positive reaction.

The titres observed were 1–4 to 1–16 in 41 of the 59 positive sera and 1–32 to 1–256 in the remaining 18.

The authors point out that these findings have an important bearing on the significance of the reaction as a diagnostic test for febrile diseases occurring in areas where endemic typhus is prevalent. *John W. D. Megaw.*

LE CHUITON, F. & BERGE, C. A propos de la présence d'agglutinines anti-Eberth, para A, ou para B, dans le sérum de sujets vaccinés au T.A.B. atteints de typhus murin nautique. [**The Presence of Typhoid and Paratyphoid Agglutinins in the Sera of Murine-Nautical-Typhus Patients who had been Vaccinated with T.A.B. Vaccine.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 103–10.

Details are given of the results of repeated Widal and Weil-Felix tests carried out on 11 patients suffering from "murine nautical typhus." Fourteen patients taken at random were examined, and only three developed no agglutinins for typhoid or paratyphoid bacilli during the course of the attack.

In one group of seven cases the typhoid titre reached a maximum ranging from 1–80 to 1–10,240, and although the Weil-Felix titre was considerably higher in five of these, it was the same (1–2,560) in one, and lower (1–1,280 against 1–10,240) in another.

In another group, consisting of two cases, the titres with both typhoid and para A bacilli rose to 1–320 or over; in one of these the typhoid titre reached 1–40,000, the para A titre 1–320, and the Weil-Felix titre 1–1,280; all on the 10th day: in the other the corresponding titres were, 1–320, 1–640, and 1–320.

In the latest group, which also consisted of two cases, the para B titres reached 1–160 and 1–320 respectively and the Weil-Felix titres were 1–640 and 1–10,240.

The diagnosis of murine typhus was regarded as certain in all the cases of the series; blood cultures were sterile in every one, and in several of them rickettsiae were isolated by guineapig inoculation.

The author points out that the sera of typhus patients are well known to have an increased power of agglutinating numerous kinds of bacteria, and that in febrile patients who have been inoculated with T.A.B. vaccine the Widal test is of little value in diagnosis. *John W. D. Megaw.*

LE GAC, P. Etude sur le typhus tropical des savanes de la haute Côte d'Ivoire. [**A Study of Tropical Typhus in the Savannahs of the Upper Ivory Coast.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 86–94.

Since December 1941, the author has studied the seasonal outbreaks of "grippe" which occur in the Upper Ivory Coast in close association with the seasonal trapping or burning out of wild rodents by the indigenous population, who greatly relish these animals as an article of diet. Certain tribes in the area regard the red rat (*Mus rufinus*) as responsible for the outbreaks of the disease, and forbid the eating of its flesh. Several Europeans who have entered the affected areas, or have come into contact with rats driven out by the prairie fires, are known to have been attacked by the disease.

Louse-transmission is regarded as unlikely on epidemiological and serological grounds. The occurrence of definite outbreaks and the absence of local sores are considered to be improbable in a tick-borne disease, and larval mites have not been found in the African savannahs. For these reasons the author believes that the rat flea, *Xenopsylla cheopis*, is the most likely vector, though he also argues that the infection probably enters the body through the mucosae, especially by ingestion of food contaminated by the hands of the rat hunters or by the urine and faeces of infected rats.

Twenty-two cases, of which one was fatal, were seen among Europeans. The rash is said to have been much less conspicuous than that of louse-borne typhus and to have differed from the rash of the tick-borne disease in being restricted to the chest. The intradermal hypersensitivity test with formolized vaccine supplied by Durand and Giroud [presumably of the epidemic typhus type] was positive in 14 of the 16 patients tested during convalescence. The Weil-Felix responses were varied; from the tables it appears that the following reactions at titres of 1–100 or over were observed in 31 tests. With *Proteus OX19*, 16 were positive (1–100 to 1–200) and of these 12 were positive also with *Pr. OXK*. With *Pr. OXK*, 13 were positive (1–100 to 1–500) and 12 of these were positive also with *Pr. OX19*. With *Pr. OX2*, all were negative at 1–100 and only two reacted at 1–50.

No significant reactions were observed among Patas monkeys, guineapigs, or rabbits, inoculated by the intraperitoneal route; and passage inoculations from these animals were negative, even among rats. Sera of inoculated monkeys and rabbits agglutinated *Pr. OX19* at titres of 1–50 to 1–150, and *Pr. OXK* at 1–20 to 1–150.

The author states that "the specific *Proteus*" of the disease has not yet been demonstrated, but that the epidemiology, symptomatology, and serum reactions suggest that the fever belongs to "the group of tropical typhus fevers (type scrub typhus of Malaya)."

[See the comment on the following paper by the same author.]

John W. D. Megaw.

LE GAC, P. Recherches sur les typhus des savanes de l'Oubangui-Chari. La maladie des Bougbous. [**Research into the Typhus Fevers of the Oubangui-Chari Savannahs. The Disease of the Bougbous.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 97–103.

The author deals with investigations carried out in 1938 into a fever which was similar in its epidemiological and clinical features to the disease described in the preceding paper. The affected area was in French Equatorial Africa, and the persons attacked had come into close contact with rats which swarmed with *Xenopsylla cheopis*. The burrows of the rats contained numerous fleas but very few ticks.

Guineapigs inoculated with the blood of infected persons had a febrile reaction lasting four or five days after an incubation period of about ten days, but there was no scrotal reaction.

The fever is said to correspond in severity to louse-borne typhus, and it is estimated that 2,000 to 3,000 persons die yearly in the area between the Cameroon border and the Anglo-Egyptian Sudan.

[The special interest of this, and the preceding, paper is that they contain evidence of the widespread occurrence in tropical Africa of a fever of the typhus group which appears to be primarily a disease of animals of the wilds. Although much of the evidence points strongly to flea transmission, the serological and experimental findings are not such as would be expected in flea-borne typhus. The author's suggestion that the disease should be classified as "tropical typhus" is not happy, but there will be general agreement with the other suggestion that more research is needed to solve the problem of the transmitting vector.] *John W. D. Megaw.*

LE GAC, P. Réaction d'hypersensibilité à l'injection intradermique de rickettsies tuées chez des sujets ayant présenté un typhus tropical. [**Hypersensitivity to Intradermal Injection of Killed Rickettsiae in Patients with Tropical Typhus.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 95–7, 1 chart.

MACKIE, T. T., DAVIS, G. E., FULLER, H. S., KNAPP, J. A., STEINACKER, M. L., STAGER, K. E., TRAUB, R., JELLISON, W. L., MILLSPAUGH, D. D., AUSTRIAN, R. C., BELL, E. J., KOHLS, G. M., WEI HSI & GIRSHAM, J. A. V. **Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. Preliminary Report.** *Amer. J. Hyg.* 1946, May, v. 43, No. 3, 195–218, 4 figs. (1 map). [21 refs.]

This paper is a preliminary report by a team of 14 workers of the U.S.A. Typhus Commission into the epidemiological and other conditions connected with the occurrence of mite-borne typhus in the China-Burma-India theatre of war from December 1944 to November 1945. The workers acknowledge the great assistance received from American and British voluntary helpers.

Towards the end of 1943, the disease was recognized as a serious military problem for the troops engaged in exercises and operations on the Assam-Burma frontier and in Burma. From early November 1943, till early September 1945, there were 1,098 cases among American and Chinese troops, with a case-fatality rate of 8·9 per cent. There were five peaks of incidence; these at first suggested that there was a pronounced seasonal rise in spring and autumn, but they were found to correspond with periods of combat, and with training operations in special areas. For example, in January 1945, there were 65,000 U.S.A. troops in Assam and Burma, yet of the 194 cases in that month all but nine occurred among 6,000 troops engaged in combat.

Certain outbreaks among Chinese troops appeared to be associated with the habit of bathing in a river on whose grassy banks the soldiers spread out their clothes to dry, and in one such locality the grassy ground was found heavily infested with mites. The wearing of shorts by the Chinese troops was also regarded as a predisposing factor.

The area most closely investigated lay along the Stilwell road from Ledo in northern Assam to Bhamo in North Burma. In a mite survey, 13 genera of trombiculid mites, including four that were new, were identified; 45 new species were found.

The following strains of *R. orientalis* were isolated by intraperitoneal inoculation of *Gerbillus gerbillus* and *G. pyramidum*:—(1) 12 from human patients; (2) 53 from pooled suspensions of trombiculid mites; (3) 8 from the rat, *Rattus*

flavipectus yunnanensis; and (4) 4 from the tree shrew, *Tupaia belangeri versurae*. Three strains were isolated from laboratory white rats, and one from the pooled tissues of 4 gerbils, which had been experimentally exposed to mite attacks in endemic regions. The preponderating mite was *Trombicula deliensis*, which was the only mite found in 24 of the pools from which infection was isolated, and which was present in every one of the positive pools.

Transovarial transmission of *R. orientalis* was demonstrated by hatching, in the laboratory, eggs of *T. deliensis* from infected localities, and causing the larvae to feed on susceptible animals.

Incompletely engorged mites sometimes became detached from the initial host and afterwards completed their meal on another animal. In four experiments with *T. deliensis* the reattached larvae caused infection in laboratory animals.

The rat and tree shrew already mentioned were the only mammals found naturally infected, though three strains were recovered from mites obtained from Sladen's roof rat (*Rattus rattus sladeni*). A complete investigation of the numerous animal hosts of *T. deliensis* was impracticable.

In the three areas along the Stilwell Road in which hyperendemicity was indicated by exceptionally high attack rates among troops, *T. deliensis* constituted 60, 74, and 96 per cent., respectively, of all the mites collected: a high incidence of this mite therefore indicates that the area should be strongly suspected. There was also evidence that areas in which cases of the disease have occurred remain risky for at least one year. *John W. D. Megaw.*

VAN DEN ENDE, M., LOCKET, S., HARGREAVES, W. H., NIVEN, J. & LENNHOFF. L. **Accidental Laboratory Infection with Tsutsugamushi Rickettsia.** *Lancet.* 1946, July 6, 4–7, 4 charts.

In spite of the strictest precautions, four persons became infected with tsutsugamushi disease in the course of work connected with the large-scale production of vaccine made from the lungs of cotton rats [see this *Bulletin*, 1946, v. 43, 435 and 436]. All the patients had been protected by Fulton and Joyner vaccine of the cotton-rat-lung type. The duration of the fever was 14–16 days in three of the cases, and at least 19 days in the fourth. One of the patients became "critically ill on the sixth day" when she had a faint heliotrope cyanosis; another was very ill on admission, and thereafter her mental and physical condition deteriorated till she became unable to take fluid by the mouth. The other two patients do not seem to have been dangerously ill at any stage of the disease. All the patients made good recoveries, and the authors conclude that as there were three deaths among five previous patients known to have had laboratory infections with *Rickettsia orientalis*, the vaccine may have had significant value in protecting against death.

From the details supplied of the clinical features of the attacks, it appears that these conformed with those often observed in the naturally acquired disease. Delirium was severe in one case, and mild or very slight in the others. In three cases there was a local lesion at the site of infection [see below] and in two of these there was an associated local adenitis. Numerous rigors and repeated falls of the temperature were features of two cases; in the other two the fever curve was of the continued type.

The Weil-Felix (*OXK*) reaction was positive in every case; in one the maximum titre was only 1–160; this was reached on the fourth day, and *R. orientalis* was isolated from the blood, taken on the second day, by intraperitoneal inoculation of mice and guineapigs. In another case the organisms were isolated from blood taken on the sixth day.

Infection of the different patients occurred in the following ways :—(1) From a prolonged bite by a cotton rat which had just received intranasal inoculation ; the incubation period was 14 days. (2) Probably by droplet infection occurring in the course of work, which involved the transfer of virulent lung suspension by a Pasteur pipette from centrifuge tubes to ampoules. By actual test it was found that bubbling, with the discharge of droplets into the air, was almost unavoidable during this procedure. (3) By a puncture of the skin, through a rubber glove, with an accidentally broken pipette which had just been emptied of a virulent suspension of the rickettsiae. A tourniquet was applied within half a minute, the wound was excised within five minutes, bleeding was encouraged and antiseptics applied. An injection of 1·0 cc. of vaccine was given at once, and on the same day 10 cc. of phenolized serum from an immunized rabbit was injected. On the next day 12 cc. of phenolized serum from a patient in the third week of convalescence was injected intramuscularly. The incubation period was 11 days. (4) Through washing by hand Petri dishes which had contained infected cotton-rat lungs. This action was in gross contravention of the rules, so the patient did not report the occurrence. The incubation period was about 17 days according to the statement made later by the patient. *John W. D. Megaw.*

SMADEL, J. E., RIGHTS, F. L. & JACKSON, Elizabeth B. **Studies on Scrub Typhus. II. Preparation of Formalinized Vaccines from Tissues of Infected Mice and Rats.** *Proc. Soc. Exper. Biol. & Med.* 1946, Mar., v. 61, No. 3, 308–13, 1 fig.

The authors mention the interesting fact that, after a number of unsuccessful attempts to produce a potent " inactive " vaccine against scrub typhus, three promising methods have been reported almost simultaneously. These were as follows ; in brackets are the dates of the original confidential reports in which they were first described :—(1) FULTON and JOYNER's rodent-lung vaccine (June, 21, 1944) [see this *Bulletin*, 1946, v. 43, 435]. (2) A tissue-culture vaccine of PLOTZ and his co-workers (September 23, 1944) [see the abstract immediately following this] ; and (3) A rodent-tissue vaccine (October 2, 1944) as described in the present paper.

White mice, white rats, or cotton rats, were inoculated intravenously with suspensions of infected yolk sacs ; the estimated dosage was 10^8 M.L.D. of *R. orientalis*. On the 4th or 5th day the animals were moribund or dead ; their lungs and spleens were homogenized and a 10 per cent. suspension in normal saline was prepared and freed from large particles by centrifugation. Formaldehyde (0·1 per cent.) and merthiolate (0·01 per cent.) were added and the suspension was stored at 5°C. for 1–6 weeks. The strength in complement-fixing antigen was titrated, though it is stated later that the potency of the vaccine could not be estimated by this procedure.

Groups of 24–70 mice were inoculated intraperitoneally with three doses of 0·5 cc. of the vaccine at five-day intervals. After two weeks the mice were challenged with varied doses of homologous rickettsiae. Large numbers of mice had to be used because of the wide range of individual susceptibility of the animals. Details are given of the results of the tests and of the standards employed in estimating the degree of immunity produced by the vaccine.

No strain of *R. orientalis* was used in preparing white-rat vaccine till it became capable of growth in a highly infective condition in yolk sacs. The infective titre of yolk-sac suspensions was easily estimated by observing the average day of death of white mice injected intravenously with 0·5 cc. of a 10 per cent. suspension. White rats were used for the preparation of the vaccine because of the large yield obtainable from each animal ; this amounted to 30–35 cc.

The authors regard their method as being preferable to the cotton-rat-lung method, because bacterial sterility was not a problem, intravenous injection is safe and simple, and white rats are easier to obtain and handle than cotton rats.

The vaccines obtained by the three methods mentioned above are said to be of comparable potency, but all are regarded as being difficult to exploit on a large scale. *John W. D. Megaw.*

PLOTZ, H., BENNETT, B. L. & REAGAN, R. L. **Preparation of an Inactivated Tissue Culture Scrub Typhus Vaccine.** *Proc. Soc. Exper. Biol. & Med.* 1946, Mar., v. 61, No. 3, 313–17.

Yolk-sac cultures of *Rickettsia orientalis* were obtained from peritoneal exudate of infected mice and used in the preparation of tissue cultures by the method of Zinnser, Plotz and Enders. The early yolk-sac cultures were poor in rickettsiae, but by selection and repeated passages a rich growth was eventually obtained, and this was found suitable for the preparation of satisfactory tissue cultures, which constituted the vaccine. Full details of the method are found in the paper.

Some of the vaccines were of low potency ; when this happened it was found that the culture flasks had not been adequately examined to ascertain their richness in rickettsiae. The most potent vaccines had " an immunity index of 3·7 to 4·5 logs ; in other words they induced protection against from 5,000 to 32,000 M.L.D.'s of *R. orientalis.*"

In one series of experiments mice received " booster " doses of vaccine, and the induced resistance was greatly increased ; for example up to 7,950 to 80,000 M.L.D.'s. This and the other two vaccines referred to in the preceding paper were regarded as being of comparable potency, but the immunity conferred on white mice by all three vaccines was obtained only by the use of intraperitoneal inoculations, never by subcutaneous injections.

It is admitted that the large-scale preparation of vaccine by the tissue-culture method " would present certain technical difficulties," but for the protection of selected personnel it " has the advantage of being a relatively clean product."

The yolk-sac method, which would be the most suitable for mass production, has never been successfully prepared ; " one reason being the deleterious effect of ether upon the antigen." *John W. D. Megaw.*

TIERNEY, N. A. **Effect of Para-Aminobenzoic Acid in Tsutsugamushi Disease.** *J. Amer. Med. Ass.* 1946, May 25, v. 131, No. 4, 280–85, 2 charts. [10 refs.]

Strikingly good results were obtained from the administration of para-aminobenzoic acid (PABA) in the treatment of 18 scrub-typhus patients in the American and Indian military hospitals at Ledo, Assam. There were 16 control cases, and almost without exception alternately admitted patients were treated in each hospital.

The chart shows that the average duration of the fever was about 10 days longer in the control group than in the treated. In three of the treated a recrudescence of the fever and symptoms occurred after the drug had been discontinued ; this second spell of fever lasted three to 14 days, but the patients were not very ill and no further doses of the drug were given. The effects of the treatment on the general symptoms were pronounced ; within two or three days the patients became alert and the headache disappeared or was greatly relieved. Four of

Comparison of the average of the highest Fahrenheit temperature each day in 16 untreated control cases of scrub typhus and in 18 cases treated with para-aminobenzoic acid (PABA).

[Reproduced from the *Journal of the American Medical Association.*]

the treated had slight bronchitis, whereas 14 of the controls had severe bronchitis. Full details are given, in tabular form, of the chief findings in the two groups of patients. The general results are shown in the following table :—

Severity of the Attacks among Treated and Controls.

	Mild	Moderate	Severe	Grave	Fatal
Indian treated (9)	8	1	0	0	0
American ,, (8)	4	3	0	1	0
Chinese ,, (1)	0	1	0	0	0
Total ,, (18)	12	5	0	1	0
Controls (16)	1	1	4	7	3

The treatment was started on the 3rd day in four cases ; on the 4th day in five ; on the 5th day in three ; on the 6th day in four ; and on the 7th day in two.

The drug was given by the mouth as a powder, to each gramme of which 10 cc. of a 5·0 per cent. solution of bicarbonate of soda was added. The dosage found most effective was 8·0 gm. initially, followed by 3·0 gm. every two hours ; the total dose was 217–357 gm. for Indian, and 217–513 gm. for American patients.

The concentration of the drug in the blood was determined by the Marshall and Litchfield method as used for sulphanilamide [see *Science*, 1938, July 22, 85] ; the level aimed at was 30–60 mgm. per 100 cc., but when the patients became afebrile the concentration was often reduced to 10–20 mgm. without recrudescence. [From a table in the paper it appears that the average maximum concentration among Indian patients was considerably higher (77 mgm.) than among American patients (56 mgm.) ; this difference suggests that the body weight of the patients may not have been sufficiently taken into account. Two

of the Indian patients who had very high maximum concentrations of 152 and 155 mgm. are said to have suffered from "confusion due to PABA," and the patient whose maximum concentration of 103 mgm. was the highest among the American group suffered from convulsions.]

There was a general tendency to leucopenia towards the end of the course of treatment; total counts of 4,000 per cmm., or less, were observed in nine of the treated and in only two of the controls. There was a satisfactory return of the leucocyte condition to normal in every case, and the treatment was never curtailed because of leucopenia. It is recommended that the total white cell count should be determined every other day; if it falls below 4,000 a differential count should be made, and if the granulocytes are less than 30 per cent. the drug should be discontinued. A total count of less than 3,000 is in itself a contraindication.

It is advised that when the blood concentration of the drug exceeds 60 mgm. per 100 cc. one dose should be omitted and the maintenance dose should be suitably reduced. The treatment should be started as early as possible, but it may be worth trying even after the end of the first week. Sulphonamides are regarded as being contraindicated; bacterial complications should be treated with penicillin.

The diet of the treated and control patients was rich in proteins, calories and vitamins; 4·0 gm. of additional sodium chloride was given, and the fluid intake was 3–4 litres daily.

In view of the results obtained in the present trials taken in conjunction with those reported by YEOMANS and his co-workers in louse-borne typhus [see this *Bulletin*, 1945, v. 42, 201], and the abundant evidence supplied by animal experiments, the authors think it likely that PABA may prove to be a general anti-rickettsial drug. *John W. D. Megaw.*

ZARAFONETIS, C. J. D., SNYDER, J. C. & MURRAY, E. S. **Immunity following Para-Aminobenzoic Acid Therapy in Experimental Tsutsugamushi Disease (Scrub Typhus).** *Proc. Soc. Exper. Biol. & Med.* 1946, Mar., v. 61, No. 3, 240–42. [Refs. in footnotes.]

Gerbils which had recovered from experimental infection with the rickettsiae of tsutsugamushi disease with the help of *para*-aminobenzoic acid (PABA), were tested six to nine months later and found immune to three different strains of *Rickettsia orientalis*, administered by the intraperitoneal route, in doses ranging from 2,140 to 31,600 lethal doses. There was only one death among the 69 gerbils used in the test. Ceylon, Calcutta, and Karp strains of *R. orientalis* were used to infect different groups of the gerbils, and the animals belonging to each group were divided into three subgroups, one of which was challenged by the homologous strain of rickettsiae, and the others by heterologous strains. Complete immunity was found to exist irrespective of the strains used in the original infection and the immunity tests, so that cross immunity had obviously been produced. The findings were regarded as showing that the action of PABA is to inhibit the growth of, rather than to kill, the rickettsiae. *John W. D. Megaw.*

BUSHLAND, R. C. **Tests against Chiggers in New Guinea to develop a Practical Field Method for impregnating Uniforms with Dimethyl Phthalate for Scrub Typhus Prevention.** *Amer. J. Hyg.* 1946, May, v. 43, No. 3, 219–29.

Trombiculid mites are a serious nuisance in many temperate and tropical regions, as well as being the vectors of scrub typhus. Some protection may be obtained in many ways, the most familiar being by dusting the socks and garments with sulphur, but this is not reliable enough when dealing with scrub

typhus. Experiments were carried out in New Guinea, using the larval mites *Trombicula buloloensis* and *Schöngastia pusilla*, which appear to be similar in their reactions to the actual vectors of scrub typhus (*T. fletcheri* and *T. walchi* have been incriminated) which cannot be obtained in sufficient numbers for experiments. [It will be remembered that PHILIP *et al.* (this *Bulletin*, 1946, v. 43, 733) regard *T. fletcheri* and *T. walchi* as synonyms of *T. akamushi* and *T. deliensis*, respectively.]

Garments were impregnated in bulk with an emulsion of 5 per cent. dimethyl phthalate, 2 per cent. soap, and water. This could be made up without any special apparatus, and after drying it left about two ounces of dimethyl phthalate in each set of garments. This gave no discomfort except a slight burning sensation in the scrotum, which was prevented by using untreated underpants.

The garments were tested by placing live mites on the material, and measuring the "stopping time", *i.e.* the time taken to paralyse the mites. If this occurred in less than 15 minutes then the garment was considered protective. Volunteers also exposed themselves in areas where mites caused scrub itch but from which typhus was believed to be absent. Impregnation gave almost complete protection up to five weeks if the garments were not laundered, and it withstood some rinsing in cold water, but protection was lost after proper laundering or after long wading in fresh or salt water.

Kenneth Mellanby.

BUSHLAND, R. C. **New Guinea Field Tests of Uniforms Impregnated with Miticides to develop Laundry-Resistant Clothing Treatments for preventing Scrub Typhus.** *Amer. J. Hyg.* 1946, May, v. 43, No. 3, 230–47.

It has been shown [see BUSHLAND, above] that uniforms impregnated with dimethyl phthalate give good protection against trombiculid mites, but that this protection is lost after the garments are laundered. Other substances toxic to mites were tried, and dibutyl phthalate and benzyl benzoate gave the best results. The benzyl benzoate, impregnated from a soap-and-water emulsion at the rate of two ounces per fatigue uniform (jacket, trousers, socks) gave practically complete protection until the garments had been laundered three times at 210°F. Dibutyl phthalate was less effective at the outset, but it withstood washing better. A mixture of equal parts of benzyl benzoate and dibutyl phthalate is advocated.

Kenneth Mellanby.

HARRELL, G. T., WOLFF, W. A., VENNING, W. L. & REINHART, J. B. **The Prevention and Control of Disturbances of Protein Metabolism in Rocky Mountain Spotted Fever. The Value of Forced Feedings of a High-Protein Diet and of the Administration of Specific Antiserum.** *Southern Med. J.* 1946, July, v. 39, No. 7, 551–7, 1 fig.

Nine children suffering from Rocky Mountain spotted fever were treated with a diet containing about twice the amount of protein present in the standard hospital diet. When necessary, supplementary feeds of high-protein liquids were given by gavage so as to bring up the total quantity of protein to 4·0 gm. per kilo. of body weight.

The general condition of the patients was observed to be much better than that of eight patients previously treated on the usual dietary. Oedema was less and there was a gain in weight during the illness in nearly every case. The serum proteins were maintained at slightly higher levels, and there was evidence that the body proteins were being depleted to a less degree.

John W. D. Megaw.

GLASGOW, R. D. & COLLINS, D. L. **Control of the American Dog Tick, a Vector of Rocky Mountain Spotted Fever : Preliminary Tests.** *J. Econom. Entom.* 1946, Apr., v. 39, No. 2, 235–40, 2 figs.

In recent years, tick-borne Rocky Mountain spotted fever has been troublesome in parts of South-eastern New York State. The vector is the American dog tick *Dermacentor variabilis*. The cases which have occurred are deterring people from using the recreational facilities which exist in this area, and the public health authorities are anxious for control measures to be devised as quickly as possible. In 1945, preliminary work was done with several insecticides, of which DDT, gammexane, pyrethrins, rotenone and nicotine appeared to be promising. Lethane 384 Special and Halowax (chlorinated naphthalenes) were less effective. Mixtures were also tried, and one promising formula was : 0·25 to 0·5 per cent. DDT plus 0·06 to 0·125 per cent. pyrethrins ; 2 quarts of this were used per acre. For application, the insecticides were dissolved in fuel oil or diesel oil, and were atomized by a paint sprayer connected to a mechanical compressor. It was proposed to try sprays applied by aeroplanes, and aerosol fogs from thermal generators, for making large scale treatments. More extensive work was planned for 1946. *J. R. Busvine.*

IRONS, J. V., TOPPING, N. H., SHEPARD, C. C. & COX, H. R. **Outbreak of Q Fever in the United States.** *Pub. Health Rep.* Wash. 1946, May 31, v. 61, No. 22, 784–5.

An outbreak of more than 40 cases in March 1946, with two deaths, in stockyard men in Texas. Investigations suggest that cattle are involved in the human infections. Clinical and serological evidence is in favour of Q fever, high complement-fixation titres to Q fever antigens being found in sera from convalescents, and rickettsia-agglutination tests being positive. The illness varied from mild fever to severe pneumonitis. *Charles Wilcocks.*

YELLOW FEVER.

GAST-GALVIS, A. Viscerotomia en Colombia. [**Viscerotomy in Colombia.**] Reprinted from *Rev. Medica.* Bogotá. 1945, Sept. & Oct., Nos. 553–554, 34 pp., 4 figs., 3 maps & 1 graph. [12 refs.] English summary.

The Colombia Viscerotomy Service was started in September 1934, and now there are 200 viscerotomy centres and the number of specimens taken has reached 22,000. When first started the object was to find, from examination of liver tissue, the prevalence of yellow fever, but the value of the procedure is not so restricted and in this article the author records the findings in other diseases also, such as malaria, sicklaemia, cirrhosis, acute yellow atrophy, tumours, etc. Of the 22,000 specimens taken, 7,302 were from children up to 4 years of age, and 1,927 from those between 5 and 9 years ; *i.e.* 9,229 (42 per cent. of the total) from those under 9 years. Among the specimens, 352 showed the changes of yellow fever, over 90 per cent. of these were from males and 136 (38·6 per cent.) were in the third decade ; only 7 were from females.

Of other diseases diagnosed from viscerotome specimens there were 2,447 cases (11·1 per cent.) of malaria (*i.e.* malarial pigment was present), most coming from the Magdalena Valley. Forty-three men and 26 women showed signs of sicklaemia or the sickle cell trait. Pathological changes of acute or subacute yellow atrophy of the liver were found in 175 subjects. Most of these came from the Bananera Zone of Magdalena, the next highest being the

south-west of Antioquia. Tuberculosis was seen in 391 specimens, 116 (29 per cent.) of which were from children under the age of 5 years and 115 from persons over 40 years. Signs of cirrhosis were present in 404, that is less than 2 per cent., and syphilitic changes in 10 only. Thirty-five showed tumours—adeno-fibroma (1), metastatic adeno-carcinoma (16, male 7, female 9), and sarcoma (2). One case of visceral leishmaniasis was seen, in Santander Department, the first to be diagnosed in Colombia. *H. Harold Scott.*

DENGUE.

DIAZ-RIVERA, R. S. **A Bizarre Type of Seven Day Fever Clinically Indistinguishable from Dengue.** *Bol. Asoc. Med. de Puerto Rico.* 1946, Mar., v. 38, No. 3, 75–80, 7 figs. on 2 pls.

[A contradiction in terms is contained in the title of this paper; if the disease is indistinguishable from dengue it cannot well be called a bizarre type of seven-day fever.]

The only important respects in which the authors regard the disease as differing from dengue are the absence of leucopenia and bradycardia; but the evidence in support of the existence of these differences is not convincing. The total leucocyte count is stated as ranging from 3,000 to 7,200 per cmm., and as the days of the disease on which the counts were made are not stated, these figures are by no means inconsistent with the diagnosis of dengue; there may have been a fall in the count during the illness. The leucocyte picture in other respects is suggestive of dengue, since "a definite lymphocytosis was observed in every instance." It is also stated that in at least 26 of the 58 cases seen at San Juan, Porto Rico, there was a tendency towards bradycardia.

Some of the chief features of the disease were:—a duration of six days, with sudden onset, accompanied by aches and pains and retrobulbar pain in every case. There were severe body pains in 70 per cent., a rash conforming to one of the types seen in dengue in 53 per cent., a biphasic fever curve in 70 per cent., and lymphadenopathy in 27·6 per cent., of the cases. The termination was by crisis or rapid lysis. It is stated that the vector and the other conditions favourable to the transmission of dengue were present. In view of these observations, and of the absence of any other explanation of the outbreak, it seems strange that there should have been any hesitation in regarding the disease as dengue.

It is also stated that Dr. W. H. Glines, of the City Hospital, San Juan, claims that dengue has been occurring in the locality "since the early thirties."

John W. D. Megaw.

BULL. U.S. ARMY MED. DEPT. 1946, July, v. 6, No. 1, 4–5. **Effective Vaccine against Dengue Fever.**

In this short note it is stated that an effective vaccine against dengue has been obtained from a strain of the virus isolated in Hawaii. This strain has undergone 32 passages through the brains of mice and has lost its power to provoke, but not to prevent, typical dengue. *Charles Wilcocks.*

POLLARD, M., LIVESAY, H. R., WILSON, D. J. & WOODLAND, J. C. **Immunological Studies of Dengue Fever and Colorado Tick Fever.** *Proc. Soc. Exper. Biol. & Med.* 1946, Apr., v. 61, No. 4, 396–8, 2 figs.

The authors have obtained experimental evidence which suggests that there is no immunological relationship between the agents of Colorado tick fever

and dengue fever. Their findings confirm those already reported by FLORIO and his colleagues [this *Bulletin*, 1946, v. 43, 737].

Two volunteers were inoculated with the virus of Colorado tick fever ; one reacted with a typical attack, the other was found to be immune as the result of an experimental attack which occurred five months previously. Both of these persons, 27 days after the defervescence of the one who was attacked, and a normal volunteer, were inoculated intradermally with serum from a dengue patient. All three responded with clinically typical dengue.

Two other volunteers were inoculated with dengue serum, and six days later had attacks of dengue-like fever lasting six days. Twenty-seven days after defervescence these persons and a normal volunteer were inoculated with the virus of Colorado tick fever. All three reacted with typical attacks of the disease.

The clinical features of the experimental attacks of the two diseases were remarkably similar, except that no rash occurred in any of the cases of Colorado tick fever. The authors point out that different strains of the same disease agent may vary to some extent in their immunological properties, so that if other strains had been used the results might not have been the same.

[In spite of the obvious clinical relationship between the two diseases it would hardly be expected that they should be immunologically identical, in view of their being transmitted by different vectors ; one case from man to man, and in the other, presumably from a lower animal to man.]

The authors refer to Bullis fever, which, like Colorado tick fever, is associated with tick bite ; they state that its aetiology appears to be different and that a further paper on the subject is in the press : they also promise a paper on the absence of immunological relationship between Bullis fever and dengue.

John W. D. Megaw.

PLAGUE.

MAGROU, E. & BRISOU, J. A propos d'une épizootie de peste dans un élevage de cobayes. [**Plague Epizootic among Breeding and Experimental Guineapigs.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 119–21.

An account is given of an epizootic of plague among laboratory guineapigs, in the course of an epidemic of plague in which rats were the source of the infection. There were peculiarities in the epizootic which seem to have some significance. At first it was not recognized to be plague. On autopsy the guineapigs presented no characteristic lesions of organs, cultures were negative and microscopic examination of spleen smears showed only small round corpuscles, some of which stained solid and some were vacuolated. These rounded bodies were Gram-negative, and it was not until the epizootic became more fatal that typical bacillary forms of *P. pestis* appeared, and cultures became positive. The authors put out the suggestion that these rounded bodies may be the only forms of *P. pestis* present in diagnostic smears of lymph nodes in the benign forms of plague and at the end of an epidemic. Cultures of the corpuscular forms, when obtained, took some 6 to 8 days to appear at room temperature.

W. F. Harvey.

MAGROU, E. Le traitement de la peste bubonique par les sulfamides (sulfadiazine). [**Treatment of Plague by Sulphadiazine.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 3/4, 113–19.

That the epidemic was due to a virulent strain is apparent from the facts that all untreated non-vaccinated persons died, and that inoculated guineapigs

died in 30 hours. Treatment, apart from adjuvant and symptomatic therapy, consisted of antiplague serum or sulphadiazine. Penicillin had proved useless, experimentally in guineapigs, and was therefore not tried. The sulphadiazine was given orally every four hours day and night, in a large volume of liquid, with at least 20 gm. sodium bicarbonate daily to keep the urine alkaline. Originally the dose of sulphadiazine was 24 or even 30 gm. on the first day, and this was gradually diminished during 10 to 15 days. The first dose was subsequently reduced to 24 or 21 gm. Treatment with serum alone appeared unavailing, and there seemed to be little distinct advantage in combining serum with the sulphadiazine. Of the 28 persons treated with sulphadiazine two died, a case mortality rate of only 7·14 per cent. *W. F. Harvey.*

CHOLERA.

GREIG, E. D. W. **The Treatment of Cholera by Intravenous Saline Injections : with particular reference to the Contributions of Dr. Thomas Aitchison Latta of Leith (1832).** *Edinburgh Med. J.* 1946, May, v. 53, No. 5, 256–63. [18 refs.]

There are many reminders in this article of how our standard therapy has been built up or originated. Transfusion of saline solution in cholera was introduced to the profession by Doctor Latta of Leith when cholera reached Edinburgh from Newcastle early in 1832. The pandemic had started in Bengal in 1823 and, for the first time, reached Europe. It is sometimes difficult to follow the reasoning for old-time methods of treatment and this is illustrated here by reference to such therapy for cholera as " actual cautery ; bastinadoing the feet ; suffocating under a feather bed." The treatment introduced by Dr. Latta, against considerable opposition, however, was based on scientific argument. He had read a report by O'Shaughnessey in the *Lancet* of the analysis of blood in cholera patients, showing the great loss of water and of its neutral saline ingredients. After several trials he decided to supply the deficiency direct into the circulation and he described his solution as artificial serum. " It was prepared by saturating water with protoxide of nitrogen holding in solution half a drachm of muriate and eight grams of subcarbonate of soda to the pound (pint) of water." Other details were included in the treatment which we have learnt to know as important. He used vapour baths to maintain the body temperature and recommended that the injection fluid should have a temperature of 112°F. " because 100°F. is too low." The effects on the patient were dramatically favourable—on the pulse, the cramps, the temperature, the respiration, the countenance, the anxiety, the thirst and the secretion of urine. In all, 156 cases of cholera were treated and 25 recovered. None would, it is considered, have recovered otherwise. There is much else of historical interest in this article and honour is also done to the collaborators of Dr. Latta, to whom it is fitting that we should pay tribute for " The wisdom that they taught us." [This paper is also a pleasing contribution to medical literature and throws an interesting sidelight on some aspects of the medical background of the early nineteenth century.] *W. F. Harvey.*

BACILLARY DYSENTERY.

BOSE, A. N., GHOSH, J. K. & RAKSHIT, P. C. **The Intestinal Excretion of Sulphanilylbenzamide in comparison with Sulphanilamide, Sulphathiazole and Sulphaguanidine : its bearing on the Efficacy of Compounds effective in Bacillary Dysentery. Part I.** *Quart. J. Pharm. & Pharmacol.* 1946, Jan.–Mar., v. 19, No. 1, 1–7, 1 fig. [19 refs.]

The authors studied the excretion of sulphonamides from the tissues into the lumen of the alimentary canal. For this purpose, the sulphonamide (0·5 gm. per kgm. body weight) was injected subcutaneously into guineapigs, which were killed 4 (or 2) hours later. The various sections of the alimentary canal were ligatured and excised. The contents of each section were washed out and made up to 10 ml. volume (in the case of the caecum to 20 ml.). The concentration of sulphonamide was estimated by the usual method. The average concentration of free sulphonamide in mgm. per 100 ml. was as follows :—

	No. of animals	Stomach	Small intestine	Large intestine	Caecum
Sulphanilylbenzamide ...	12	2·9	5·7	4·9	23·1
Sulphanilamide	7	5·8	6·2	2·2	6·2
Sulphathiazole	7	4·5	35·2	1·7	4·7
Sulphaguanidine	5	11·3	3·5	1·4	4·5

There was considerable variation between the different animals. Apparently the excretion of sulphathiazole into the small intestine, and that of sulphanilyl-benzamide into the caecum, are relatively high. The bearing of these results on the treatment of dysentery is discussed. [Presumably the amount of sulphonamide found in the lumen of the gut following oral administration would be much higher than the amounts recorded above.]

F. Hawking.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

SHRAPNEL, B. C., JOHNSON, C. M. & SANDGROUND, J. H. **Oral Emetine in the Treatment of Intestinal Amebiasis. A Preliminary Report.** *Amer. J. Trop. Med.* 1946, May, v. 26, No. 3, 293–310. [16 refs.]

After a very brief account of the introduction of emetine as a therapeutic agent in amoebiasis the authors state that they consider it a toxic and even a dangerous drug when administered hypodermically, and therefore its dosage by this route must be limited to an extent which does not allow of complete parasitic sterilization of *E. histolytica* gut infections. It is surprising that more attention has not been devoted to developing the alkaloid for oral use ; the currently available forms such as emetine-bismuth-iodide, emetine-antimony-iodide, etc., cause salivation, nausea and vomiting, and have not, on the whole, been successful. In their attempt to give emetine in greater dosage, without the usual side effects, the authors had 1/3 grain of emetine hydrochloride put up in "enteric-sealed" tablets ("Enseals", Lilly) which are designed to resist digestion for 3 to 4 hours after ingestion, and thus to liberate the drug in the lower bowel and not in the stomach. Twenty patients with intestinal amoebiasis were treated with this preparation ; the patients included

members of both sexes, and were Latin Americans, British and North Americans, the two youngest patients of the group were 1 year and 8 months and 1 year and 9 months old respectively, and the oldest 56 years. The diagnosis in each case was substantiated microscopically, and a number of examinations, including daily blood pressure readings and electrocardiographic examinations every three days, were made before, during, or after treatment. Three types of dosage were employed. Group I (7 cases) received one Enseal thrice daily for 12 consecutive days (a total of 12·0 grains emetine hydrochloride by mouth); Group II (6 cases) received two Enseals thrice daily for six days (also a total of 12·0 grains of emetine hydrochloride); Group III (7 cases) had larger gross dosages which varied from one individual to another, the greatest amount given to an adult being 23 grains of the drug over a period of 19 days. The data relative to each group are set out in extensive tables.

With each dosage employed, isolated incidents of abrupt vomiting unaccompanied by nausea or colic were encountered on rare occasions. These were probably attributable to chipped tablets, and ceased when these were discarded. One patient in Group I, two from Group II and three from Group III were found still to be infected after completion of treatment; all these were variously re-treated with Enseals, one at least unsuccessfully in so far as parasitic cure is concerned, while some of the remainder were observed over an inadequate period to determine success or failure in this matter. The authors conclude that emetine given in this manner is at least not seriously toxic or dangerous, that their results are encouraging, and that they warrant more extended investigation of this mode of treatment. *A. R. D. Adams.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

GRENOILLEAU, G. L'épidémie de fièvre récurrente en Algérie en 1944. [**The Outbreak of Relapsing Fever in Algeria in 1944.**] *Bull. Acad. Méd.* 1946, v. 130, Nos. 6, 7 & 8, 144–5.

This paper describes an outbreak of relapsing fever in Algeria between November 1944 and October 1945, during which period 15,606 cases were reported.

The authors point out that, whilst large scale epidemics of *T. recurrentis* infections had been rare in Algeria since 1904, apart from light outbreaks in 1924, 1927 and 1928, the present one was not unexpected, since Tunisia had been attacked by the disease several months before Algeria. Since the first cases, appearing in Sfax in January 1944, spread widely through Tunisia, it was inevitable that Algeria should be attacked eventually.

The epidemic probably originated in Fezzan where, as far back as 1905, there had been a serious outbreak of louse-borne relapsing fever, which had been the origin of the North African infection studied at that time by NICOLLE.

From April 1943 until the end of 1944, a number of cases were recognized in Fezzan. Tunisia became affected at the beginning of 1944, and cases began to appear in Southern Algeria, adjacent to the El-Erg neighbourhood on the Tunisian border.

In November 1944, Algeria reported the first cases in the Department of Constantine, bordering on Tunisia. This department was rapidly invaded, to be followed soon by the departments of Algiers and Oran. In two months the disease had travelled throughout the 600 miles of Algerian territory from East to West, to attack Morocco in February 1945. Regions to the East remained completely free, and no outbreak was reported from Egypt.

The largest number of cases in Algeria was reported in March, barely three months after the epidemic had begun. The authors note particularly the extremely fulminant course of the outbreak. They believe that the reported cases scarcely represent one-tenth of the true incidence.

The mode of infection did not call for any special comment, and mortality was never reported to be striking. In the whole territory, it averaged about 3 per cent. In the hospital of El-kettar, in Algiers, only 32 of 2,028 persons suffering from the disease died (1·6 per cent.). Mortality in Europeans was almost negligible.

Even though the death-rate was not striking, a number of complications were reported, namely: prolonged digestive disturbances, jaundice, interrupted pregnancies, haemorrhagic syndromes, iritis and other ocular complications.

Treatment with arsenicals (Stovarsol, Novarsenobenzol and Mapharsen) gave good results.

The preventive measures prescribed included: compulsory notification of cases; immediate sterilization of the blood of infected persons, by the use of arsenicals; thorough washing of patients and disinfestation of their clothes; and the use, when available, of powdered insecticides (AL 63 and DDT).

H. J. O'D. Burke-Gaffney.

CHIAO, S. M. **The Epidemiological Investigation and Control of Relapsing Fever Outbreak at Tung Chi, Kweichow, 1940.** *Acta Brevia Sinensia.* 1945, No. 9, 4–13, 1 fig. [17 refs.]

A description of an epidemic of louse-borne relapsing fever occurring at Tung-Chi, Kweichow, during 1940.

The author first went to Kweichow Province in 1939, and during that year 37 sporadic cases of relapsing fever were recorded from 11 districts. There was no serious outbreak, however, until March 19, 1940, when an epidemic of "fowl nest fever" was reported at Tung-Chi. The disease is said never to have been epidemic there until recently.

An examination of blood smears from 549 cases of "fowl nest fever" [the reason for this name is not given] showed the presence of spirochaetes in 161, whilst in 1,133 cases of other types of fever, spirochaetes were found in only three patients. A total of 113 inhabitants of the epidemic zone were examined for lice, and all, without exception, were infested with body-lice; 75 per cent. were also infested with head-lice. Spirochaetes were found in 19 out of 32 body-lice examined, but 5 head-lice were negative.

It is estimated that there were at least 5,500 cases of relapsing fever in this district during the epidemic; the number of deaths was about 2,350, a case fatality rate of 42·7 per cent. There were no marked variations in age or sex distribution of cases, but it was most prevalent among farmers. A study of the distribution of cases showed that the heaviest infection was around the district connected with Chungking and Kweiyang by highways, suggesting that it was an importation. The epidemic reached its height in late winter and early spring and died down during the summer.

Attempts were made to eradicate lice by the use of domestic boilers, and wooden barrels for delousing isolated families (wine-distilleries were used for this purpose in the larger villages), and by the regular changing of straw at coolie-camps. Against head-lice pyrethrum ointment was found to be satisfactory.

In this outbreak 282 patients were treated by intravenous injections of neoarsphenamine. The majority showed a quick response, with a crisis in 8 to 24 hours, but it was not possible to following up the cases to determine their subsequent history.

E. Hindle.

YAWS.

HUDSON, E. H. **Treponematosis.** Reprinted from *Oxford Loose-Leaf Medicine.* Chapter XXVII–C. 1946, June 14, pp. 9–122. [134 refs.] Ohio University, Athens, Ohio.

In this study—a task which has extended over 20 years—the author has summarized, in a convincing manner, the current views regarding the unity, or otherwise, of the diseases due to the spirochaete, *Treponema.* He argues in favour of the unitarian theory, claiming that there is one species only, *pallidum.* Propagated both by the venereal and non-venereal routes, forms of disease caused by this organism are characterized by early and late stages separated by a latent period, with characteristic pathological response in human tissues; they are diagnosable by serological tests and are susceptible to treatment with heavy metals and penicillin.

Treponematosis is so universal that it has been called the "disease of one thousand names." Sometimes it is known as framboesia (raspberry), sibbens (berry), pustulis, bubas, pinta; sometimes as yaws (Africa), irkintja (Australia) and bejel (Syria); sometimes as syphilis or, more fancifully, as the "disease of St. Job."

In times past treponematosis had been confused with button scurvy, scabies, variola and venereal leprosy. It has been called the "foreign disease," morbus gallicus, Neopolitan disease, Amboina pox, mal di Fiume, or the Crimean disease. In Dalmatia it has paraded as skerljevo; in Denmark as radesyge and in Greece as spyrokolon. The adult venereal form and the non-venereal childhood acquired form have borne separate names simultaneously in the same country. In the Balkans there is syphilis and skerljevo; in Australia kirkni and irkintja; in Arabia franghi and bejel. At other times a particular manifestation has been dignified by a name, such as gangosa in Guam and pinta in Mexico.

Treponema should be adopted as the generic name for the microscopic parasite. No organism possesses a more legitimate name than this, which was coined for it by Schaudinn, its discoverer. It is a very fragile creature, killed by the weakest antiseptics and especially sensitive to soap solutions. Something in the nature of host tissue appears to be necessary to maintain its virulence. Its uniform reversion and resumption of saprophytic nature in culture media is in harmony with this view.

Two things appear certain, one that it was in the remote past *Treponema* became established as a parasite of man and that it must have done so in some moist, hot climate conducive to its existence, and the other that it first lodged in the tissues as the result of some abrasion of the skin. Possibly this occurred in Africa, where the necessary conditions obtain and where yaws is a native African word which in its reduplicated form—ya-ya—turns up in the Caribbean as a legacy of the African slave days. In the African there is displayed a complete and detailed picture of juvenile and rural treponematosis which has resulted from that first encounter.

As long as treponematosis remained in the most tropical zones, such as Central Africa and the Pacific Islands, it retained its character as a disease of childhood, which affected everybody in the villages. This type did not commence in a chancre, but with florid skin eruptions, and it did not end in aneurysms and paresis, but in gangosa, pinta-depigmentation, skin ulcers and periosteal gummata. The climate was favourable for the treponemata to live and multiply in the unclothed skin. In the dry areas of the tropics the external characters of treponematosis changed.

In cooler and drier climates the skin surface offers less favourable conditions for the propagation of the treponema. Sometimes, as in Jamaica, there is a

seasonal swing and the organism can persist on the surface only during the rainy season. In drier climates treponemata appear more abundantly in the axilla, popliteal space, perineum and external genitalia. Lesions of the mucous membranes, which were rare as long as the skin lesions were florid, become more numerous in these conditions, appearing as " mucous patches," " snail tracks " or kidney-shaped ulcers on the fauces, palate or pharyngeal wall. Such is the treponematosis of Arabia and mountain areas today, whilst Ramsay in Assam observed 20 years ago that heat and moisture appeared to be the main factors in producing the characteristic lesions of treponematosis in that area.

Treponematosis did not remain confined to torrid zones. During its migration north its character altered by changing its pattern from a juvenile, non-venereal disease to one of adult venereal infection. The forces of environment made it difficult for the parasite to remain confined to the skin, and drove the eruption towards the mucosa of the mouth and vagina. In this manner sexual intercourse afforded the common channel of infection.

In a specially important section, labelled *Christopher Columbus*, the author pours scorn on the familiar recapitulated tale of the introduction of syphilis from the New World. It is argued that the evidence in support of this story is very weak and that it is absurd to suppose that, by action of the comparatively small number of suspects involved, the seeds of an epidemic of syphilis of such magnitude or of such virulence could have been sown. Arguing from analogy is at best a risky procedure, but the author is not deterred by this, and refers to the accepted views on the genealogy of the horse from *Eohippus*, on which the evolutionary development of the modern animal is generally based. In much the same way all the intervening and transitional steps between yaws and paresis can be demonstrated in European history within the compass of a few centuries.

The remainder of this exhaustive paper is replete with the oft-quoted distinctions between yaws and syphilis, the trend of which is to back up Jonathan Hutchinson's dictum " whenever an Englishman contracts yaws abroad he comes home with syphilis."

A similar attitude is adopted in the consideration of pinta, which is regarded as the depigmentation commonly associated with syphilis and yaws. The parasite, *T. carateum*, is indistinguishable either from *T. pallidum* or *T. pertenue*. Pinta starts out exactly as many other cases of juvenile treponematosis. It is not true to state that it is confined to Central and South America, as it would seem that this de-pigmentation is prevalent in the whole American hemisphere. Lieberthal has found three cases in Chicago, and it is reported from the Argentine ; American observers in Guam are finding it there now. Therefore pinta may occur anywhere where there is treponematosis, especially of the juvenile and untreated type. That aortitis, adenopathy, juxta-articular nodules and other late signs of spirochaetosis are found in association with pinta is considered sufficient to clinch the argument.

Finally, there are four considerations which recommend the author's views of acceptance of treponematosis as a world-wide disease. The first is a classification of nomenclature by resolving several diseases into one. This is a usual procedure, as exemplified in other diseases such as tuberculosis in its various manifestations ; plague (sylvatic and human) ; borreliasis (tick- and louse-borne) ; and yellow fever (jungle and urban, African and American). Such classification has resulted in a better understanding of these diseases.

Secondly, the comprehensiveness of treponematosis tends to produce a new and less provincial attitude.

Thirdly, research in treponematosis is now handicapped by compartmental thinking, and the assumption that yaws and syphilis are different diseases is a

barrier to any comprehensive programme. Yaws has much to offer as a field for study of the ecology and biology of the treponema.

Lastly, if treponematosis is a disease of all mankind, it should be recognized as such by epidemiologists, health officers, social hygienists and civil governments, and such questions as sanitation, social habits, economics and laws are involved. Different educational procedures should be integrated. It is an illusion to hope for a syphilis-free civilization while yaws remains rampant in wide areas of the world.

[We have presented the author's views in an unbiased manner. He acknowledges himself quite patently as a disciple of that staunch unitarian, the late Admiral Charles S. BUTLER, whose "*Syphilis Sive Morbus Humanus*" (1941) is so well known. No doubt equally cogent arguments can be advanced against this view. But that the present affords a good occasion to review the subject as a whole, which has been so thoroughly and eloquently done in this treatise, there can be little doubt.] *Philip Manson-Bahr.*

FLOCH, H. & DE LAJUDIE, P. Traitement pratique du pian par la pénicilline en suspension dans l'huile d'olive. [**Treatment of Yaws by Penicillin suspended in Olive Oil.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 115.* 1945, Oct., 8 pp.

Solutions of sodium penicillin in distilled water, in saline, or in 5 per cent. glucose lose their activity within 48 hours, even when kept in the cold; moreover, when administered they are rapidly excreted. The authors found that in olive oil the drug could be kept for 10 days in a frigidaire and still be active and also that, by being suspended in oil, it remained longer in the body.

In practice 100,000 Oxford units are shaken for 10–15 minutes in 10 cc. of the oil previously sterilized in an autoclave. Four cases of yaws are recorded in which about 15,000 units were injected intramuscularly each day for 7 days, a total of a little over 100,000 units. By the third day the lesions had cleared or were fast disappearing, and by the end of a week "clinical cure" was complete, but serologically the Meinicke and Vernes reactions remained unchanged, or were slightly reduced and continued so during subsequent periods of observation [but these were short, two months in two patients and only one month in the other two]. *H. Harold Scott.*

LEPROSY.

IBARRA PÉREZ, R. & GONZÁLEZ PRENDES, M. A. Incidencia de la lepra en Cuba según la raza. [**Racial Incidence of Leprosy in Cuba.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1946, v. 3, No. 1, 19–24. [11 refs.]

[It is difficult to reconcile the statements in the letterpress of this article with the figures presented in their support.] The authors claim at the outset that Cuba differs from other Latin-American countries in that there is no half-caste population from crossing of the Spanish blood with that of the original indigenous inhabitants, because the latter were exterminated in the 16th century. Nevertheless the percentage of half-castes from admixture of white and negro bloods is high. Whites number 3,553,312 (74·4 per cent. of the whole), negroes 463,226 (9·7), half-castes 743,115 (15·5), and Chinese 18,929 (0·4 per cent.). The lepers among these number respectively, whites 1,649 [4·6 per 10,000], negroes 340 [7·3], half-castes 408 [5·4], and Chinese 30 [15]. In the face of

these figures [the totals only are given, not the incidence by population] the authors claim that " race is not a predisposing factor because the incidence is the same among the different races composing the population." The " slight increase " among the black and yellow races is due, they say, to economic and hygienic conditions—the people living in poor, ill-fitted dwellings, devoid of sanitation, and overcrowded ; they are badly fed and predisposed to disease by the presence of malaria, syphilis, tuberculosis and parasitic infection. The authors next proceed to estimate the incidence, exclusive of Oriente Province, in which the population is given as 1,362,489, and they show that among the whites there are 1,313 cases [4·8 per 10,000], among the negroes 181 [6·0], among half-castes 236 [6·1], and among Chinese 28 [17·4]. They conclude from this that " the slight increase in the non-white races is due to the causes mentioned above." Lastly, they give analogous statements on Oriente itself: 337 lepers among 835,360 whites [4·0 per 10,000], 159 among 161,712 negroes [9·8], 172 among 356,532 half-castes [4·8], and 2 among 2,885 Chinese [6·9].

Commenting on these figures the authors state : " The increased percentage of negro lepers occurs exclusively at the cost of the diminution in the white population. The half-castes and the Chinese retain the same percentage incidence." [It will be seen that the figures do not bear this out. In the Tables given the totals and the percentages of the whole are stated, not the morbidity by race. The figures given (by the abstracter) in square brackets have been calculated on the total figures in the text.] *H. Harold Scott.*

TRESPALACIOS, F. & GONZÁLEZ PRENDES, M. A. Primeros síntomas y edad probable de contagio en lepra. Estudio de 315 casos asilados en el Hospital San Lázaro de la Habana. [**Earliest Symptoms and Probable Age of Infection in Leprosy.**] *Rev. Sifilografia, Leprologia y Dermatologia.* Marianao, Cuba. 1946, Jan., v. 3, No. 1, 38–48.

This record is based on a study of 315 patients in the San Lázaro Hospital, Havana ; 233 were males, 82 were females ; 200 were whites, 46 were negroes, 50 were half-castes, and 19 were Chinese ; 262 were Cuban born, 53 were from abroad.

Sometimes the first symptoms appeared suddenly (after months or even years of incubation) as, for example, a rhinitis with epistaxis ; at other times and more commonly, insidiously, with maculae or some cutaneous manifestation—erythema, pigmentation, or an achromic patch. In a Table giving the first symptoms it will be seen that 60 started with erythematous maculae, 25 with infiltration of the ears, 23 with patches of anaesthesia, 17 with pigmented maculae, the same number with systemic symptoms such as headache, fever, lassitude, etc. [ROGERS and MUIR, in an analysis of 252 cases, found achromic maculae and anaesthetic patches as the first symptom in 188 or 74·7 per cent.]. In 208 patients (63 per cent.) the symptoms appeared first before the age of 25 years ; 37 within the first 10 years of life ; the largest number in any single year was 26 in the 20th. The probable age when infection was contracted is also given, in quinquennia, the figures up to age 50 years being 3, 31, 60, 66, 45, 30, 20, 20, 9 and 13. [In another table six are said to have contracted the disease " soon after birth," in the first year of life.] The average age of contagion worked out at 18 years and the appearance of symptoms at 23 years. Of the total, 253 (80·3 per cent.) suffered from the lepromatous form, 49 (15·5 per cent.) from a " non-characteristic or non-specific type ", and 9 from the tuberculoid type [these total 311, not 315]. During 1945, there were 31 deaths at the hospital ; 15 patients escaped, four were released on parole and there were 16 re-admissions. *H. Harold Scott.*

JAQUETI DEL POZO, G. La ginecomastia en la lepra. [**Gynaecomastia in Leprosy.**] *Revista "Fontilles."* Valencia. 1946, Jan., No. 4, 283–95, 4 figs. on 1 pl. [29 refs.]

RODRIGUEZ PASCUAL, C. Alteraciones nasales en la lepra. [**Nasal Changes in Leprosy.**] *Revista "Fontilles."* Valencia. 1946, Jan., No. 4, 297–303, 8 figs. on 2 pls. [19 refs.]

DUEÑAS, C. & ABAD, R. Serologia de la lepra. [**Serum Reactions in Leprosy.**] *Revista "Fontilles."* Valencia. 1946, Jan., No. 4, 307–18, 1 fig. [28 refs.]

Three tests carried out with the serum of lepers are recorded: Eitner's complement fixation, Rubino's test with sheep's cells, and Muchow and Lewy's flocculation with leproma extract.

Sera from 249 patients with various types of leprosy were tested, and the results are summarized thus :—

International Classification	Number of Patients	Reac. Eitner — Positives	Per cent.	R. Rubino — Positives	Per cent.	R. Muchow — Positives	Per cent.
L1	2	—	—	1	50	2	100
L2	43	13	30·2	28	65·1	35	81·3
L3	61	19	31·1	42	68·8	51	83·6
NI	6	—	—	1	16·6	1	16·6
N2	18	5	27·7	13	72·2	13	72·2
N3	52	10	19·2	39	75	38	73
L2 N2 ...	20	10	50	15	75	19	95
L2 N3 ...	15	7	46·6	8	53·3	13	86·6
L3 N2 ...	6	3	50	6	100	6	100
L3 N3 ...	26	14	53·8	22	84·6	24	92·3
Total ...	249	81	32·5	175	70·2	202	81·1

With the Muchow and Lewy test, 81·1 per cent. of the specimens were positive in some degree. The percentage distribution of positive results according to intensity of reaction is shown in the following table :—

	+	++	+++	++++
L1	—	100	—	—
L2	16·2	32·2	23·2	11·6
L3	16·3	32·7	24·5	9·8
N1	16·6	—	—	—
N2	16·6	22·2	27·7	5·5
N3	5·7	25·0	30·7	11·5
L2 N2 ...	10·0	30·0	45·0	10·0
L2 N3 ...	—	20·0	47·3	20·0
L3 N2 ...	—	—	33·3	66·6
L3 N3 ...	—	7·6	45·3	38·4
Total per cent.	10·4	25·3	30·5	14·8

These same sera were tested also for syphilitic and tuberculous reactions. For the former the Wassermann, Hecht, M.K.R. II, Kahn, Leiboff and Hinton ;

for the latter the Besredka, Daranyi and the Matefi. The authors conclude that among those of the same clinical type of leprosy, the number and intensity of the reactions depend on the length and severity of the disease, and that when the results of the leper sera coincide with those of the syphilitic tests, both being positive, there is probably a dual infection of leprosy and syphilis.

H. Harold Scott.

GUILLEN PRATS, J. & GOMEZ LUCAS, R. Penicilina y lepra. [**Penicillin in Leprosy.**] *Revista "Fontilles."* Valencia. 1946, Jan., No. 4, 305–6.

The sodium salt of penicillin has been tried in a severe case of leprosy L_3 with, so far, good effect. The patient was a man of 43 years who had suffered from the disease for 16 years. His nose and ears were much enlarged by numerous lepromata, eyebrows gone, interstitial keratitis in both eyes, especially the left, lepromata of shoulders, thighs and hands, many confluent; oedema and infiltration of legs and feet. Bacilli were present in the nasal mucus and in the skin lesions. Red cell sedimentation 65 mm. in one hour, 110 in two hours. The penicillin was injected intramuscularly, 10,000 Oxford units every three hours. Early injections caused febrile reactions disappearing in 24 hours; there was much local pain. By the third day the patient stated that he felt better, and the vascularization of the conjunctiva and cornea was less. After 300,000 units the oedema of the feet and legs was reduced, the lepromata of the shoulders were smaller, he was much more cheerful and no longer suffered from insomnia. For 12 days the drug could not be obtained and the treatment had to be suspended. It was then resumed till he had had two million units. With this new series the early injections caused even greater febrile reaction than had the first but this reaction ceased in 36 hours and was never serious enough to call for suspension of the treatment. By this time the lepromata were reduced, oedema of the feet and legs was no longer observed, eye lesions were less marked and the euphoria continued as the patient was convinced of the improvement. The blood sedimentation rate was now 42 and 81 in one and two hours respectively. The amelioration had continued for 1½ months at the time of report. The authors acknowledge that this interval is short and think that higher doses should be given before the final assessment of the value of penicillin is made, but so far they are favourably impressed by its action in leprosy.

H. Harold Scott.

DE WILDEMAN, E. **A propos de médicaments antilépreux d'origine végétale. IV. Des *Strophanthus* et de leur utilisation en médecine.**

This book is reviewed on p. 974.

HELMINTHIASIS.

GAMA, C. & DE SÁ, J. M. Esquistosomóse medular. (Granulamas produzidos por ovos de esquistosoma Mansoni (Schistosoma Mansoni) comprimindo a medula, epicone, cone, e cauda equina—Paraplegia flácida). [**Schistosomiasis of the Spinal Cord. Granuloma due to Ova of *Schistosoma mansoni*, pressing on the Lower Spinal Cord.**] *An. Facul de Med. Bahia.* 1944–45, v. 4, 187–251, 6 figs. [234 refs.]

Spinal symptoms have been recorded more than once in patients infested with *Schistosoma*, but rarely has the cause been proved to be the helminth or its ova. DAY and KENAWY recorded a case in 1936 [see this *Bulletin*, 1936,

v. 33, 951] in which *S. haematobium* was the agent, and there is another by HOFF and SHABY in 1939 [this *Bulletin*, 1940, v. 37, 147], in which intestinal lesions were present and ova of *S. haematobium* found in the urine. In the latter case ova were *not* found in the spinal cord and all that can be said is that "myelitis, with mental disturbance, occurred in a patient infested with *S. haematobium*."

S. japonicum ova have also been found in the human brain [noted in BUMKE and FÖRSTER's *Handbuch der Neurologie*].

The case here recorded is that of a man aged 42 years with signs of flaccid paraplegia. His father had died of tuberculosis and several relations had had cancer. The paraplegia came on when he was in good general health and comparatively rapidly, with pain in the loins and legs, formication, retention of urine and faeces, and loss of patellar, abdominal, cremasteric and plantar reflexes. The blood showed an eosinophilia of 16·3 per cent. [no details as regards totals of leucocytes are given, and the percentage as stated adds up to 119·4]. Radiological examination after injection of lipiodol indicated obstruction beginning at the 6th dorsal vertebra and extending to the 12th, where it became complete. A little later, complete blockage of the spinal canal was found to be at the level of the 2nd lumbar vertebra.

Operation was decided upon and a swelling was found at this level; it was thought at first to be cystic, but puncture did not draw off any fluid. A portion was taken for section and the tumour removed. It was found to consist of five small nodules, in the centre of each of which was a foreign body which proved to be an ovum of *S. mansoni*. The patient was treated with fouadin, stibosan, stibenyl, anthiomaline, and, when these could not be obtained, with tartar emetic in 1 per cent. solution, and deep radiotherapy. There was good improvement; within three weeks voluntary movements were returning in the toes and leg muscles and even before this he was regaining control of the bladder.

The actual source of infestation was not determined with certainty. The patient had bathed in waters in which the intermediate host, *Australorbis glabratus* or *Planorbis olivaceus*, was known to be present, in 1926, and in 1941, 1943 and 1944, and after the first at all events he had suffered from "severe intestinal disturbance and frequent attacks of diarrhoea."

H. Harold Scott.

GONZALEZ RINCONES, P. Stibioterapia per os. [**Antimonial Medication by Mouth.**] *Gac. Med. de Caracas.* 1945, Sept. 15, v. 53, No. 17, 127–41, 11 figs. & 2 charts.

There are obstacles to administering tartar emetic by mouth because the gastric juice breaks it down, since the HCl is stronger than the tartaric acid of the antimony potassium tartrate, and more toxic compounds are formed. On the other hand there are drawbacks to intravenous administration. The salts are changed by heat, and are difficult to sterilize, in children and in some women the vein is not always easy to find, the patient has to attend at the doctor's surgery and this he often fails to do regularly.

The author, has, therefore, aimed at finding some way of administering the drug by mouth without causing intolerance or signs of antimony poisoning. He has had pastilles made, combining the drug with atropine, 1/20 mgm. to every cgm. of the tartar emetic, to counteract its stimulant effect on the vagus, and adding "a small proportion of vitamin B_1" (thiamin) and coating the whole with keratin to allow it to pass undecomposed into the intestine. He has used these for treatment of infestations by *Schistosoma mansoni*, observing by X-ray the passage of the pastilles until they are dissolved and absorbed in the large intestine. Two cases are quoted and X-ray photographs are reproduced showing the progress of the pastilles. He gave four tablets (or pastilles)

the first day, two doses of two each, 8 on the second, 8 on the third, 10 on the fourth (all colic and tenesmus had disappeared by this time), 12 on the fifth, and so on. By the 10th day 120 pastilles had been taken and, in all, 1·2 gm. of the drug. All clinical signs had cleared. Slight gingivitis, with sialorrhoea and a metallic taste indicated that the drug had been absorbed. The maximum dose in a day should be 2 cgm. per 10 kilos, given in two or three doses in the 24 hours. *H. Harold Scott.*

JANSEN, G. Experiências sôbre a profilaxia da esquistosomose mansoni no estado de Pernambuco. Nota prévia. [**Prophylaxis of** *Schistosoma mansoni* **Infection in the State of Pernambuco. Preliminary Note.**] *Brasil-Medico.* 1946, May 18 & 25, v. 60, Nos. 20/21, 177–9, 3 figs.

This account deals with the Catende Municipality, where was installed the first centre for combating schistosomiasis in Brazil.

Preliminary examination of the faeces of 6,559 persons showed that 3,482 (52 per cent.) were positive. For initial experiment 50 patients were subjected to stibin intramuscularly and a like number to each of antimonyl, stibetine, and 1 per cent. tartar emetic, all administered intravenously. The numbers cured were, respectively, 11, 28, 37 and 49 ; cure implying three consecutively negative examinations.

Treatment was now started in earnest and up to December 1945 [the date of beginning the work is nowhere stated], of 1,348 receiving tartar emetic 1,159 (85 per cent.) were cured ; of 292 receiving stibetine intramuscularly 42 (14·3), of 169 receiving it intravenously 97 (56·8) ; of 12 receiving antimonyl intramuscularly 5 were cured, of 117 intravenously 39 (33·3) ; of 50 receiving stibin intramuscularly 11 (22 per cent.). Altogether of 1,988 patients treated 1,353 (68 per cent.) were cured. [No details of the composition of these drugs are given.]

Tanks for washing clothes and public baths were installed and also house latrines, for of 1,252 registered houses, 424 had no sanitary installations of any kind.

Examination of the vector, *Australorbis centrimetralis*, in various waters was carried out in July 1943, and again in December 1945. In 1943, of 752 from the Rio Pirangi 10 were positive ; of 607 from the Rio Panelas 16 (or 1·32 and 2·63 per cent. respectively) ; in 1945 the numbers examined were 64 and 90 and the numbers positive 0 and 2 respectively, lime having been applied in the interval. *H. Harold Scott.*

LOBO, R. A profilaxia da esquistosomose na Bahia. [**Prophylaxis of Schistosomiasis in Bahia.**] *Brasil-Medico.* 1946, Jan. 5 & 12, v. 60, Nos. 1/2, 9–14.

Schistosomiasis mansoni constitutes, in parts of Brazil, a scourge as serious as malaria ; nevertheless the Health Authorities " do not, or pretend they do not, see how serious the question is." In the past six years, 1940–45, the local laboratory returns of examinations for ova have been 26·6, 40·0, 32·5, 32·3, 24·0 and 43·7 per cent. positive. The author adds : " Of a total of 661 examinations made, 83 were positive—32 per cent." [If these last figures are correct, and they refer to 12 consecutive years, the total is very small and the percentage is not 32 but 12·5.] Another table shows 2,223 examinations with 372 positive (16·7 per cent.), of which 1,594 were from males with 287 (18 per cent.) positive, and 629 from females, 85 (13·5 per cent.) positive.

Preventive measures suggested are along the usual lines : Establishment of Sanitary Posts for free treatment of patients, installation of privies at all

schools, propaganda by handbills, lectures, cinema films; elimination of *Planorbis* from the waterways, and relief of poverty, malnutrition and overcrowding. *H. Harold Scott.*

LIGER & SCHNEYDER, R. Kystes hydatiques chez les indigènes Nord-Africains. [**Hydatid Disease in North Africans.**] *Semaine des Hôpitaux de Paris.* 1946, July 21, v. 22, No. 27, 1280–84, 8 figs.

DAVIES, J. A. **Echinococcal Cyst arising from the Prostate.** *Canadian Med. Ass. J.* 1946, Mar., v. 54, No. 3, 268–71, 1 fig.

POST-GRADUATE MED. J. 1946, July, v. 22, No. 249, 203–4. **Casoni Test. A Review.**

BERBERIAN, D. A. **Treatment of *Hymenolepis nana* Infection with "Acranil."** *Amer. J. Trop. Med.* 1946, May, v. 26, No. 3, 339–43. [15 refs.]

"25 cases of *Hymenolepis nana* infection in children were treated by a synthetic acridine derivative 'Acranil'. The night before the administration of Acranil, the children were each given 0·1–0·2 gm. Calomel as aperient. The following morning Acranil was given on an empty stomach in 0·1–0·5 gram doses according to age. Three hours later a saline purge was administered. Treatment with Acranil was continued in smaller doses for three more days without any further purgation. 23 out of 25 children treated by this method remained free of worms for 14 days."

BROWN, H. W. **The Use of Gentian Violet in Children infected with *Ascaris lumbricoides*.** Reprinted from *J. Pediatrics.* 1946, Feb., v. 28, No. 2, 160–64. [14 refs.]

"1. Gentian violet therapy for ten consecutive days did not produce findings suggestive of migration of *A. lumbricoides* or of intestinal or pharyngeal obstruction in twenty treated children. It appears, therefore, that gentian violet is not a specific irritant to *Ascaris*.

"2. A 37 per cent. reduction in the *Ascaris* egg count following gentian violet therapy suggests that this substance is slightly effective against *Ascaris*."

BROWN, T. McP., STIFLER, W. C., Jr. & BETHEA, W. R., Jr. **Early Filariasis.** *Bull. Johns Hopkins Hosp.* 1946, Mar., v. 78, No. 3, 126–54, 9 charts. [31 refs.]

This paper deals with the early clinical manifestations of filariasis as determined by the study of three groups of American servicemen; two of these groups served in the South Pacific islands (Tonga-tabu and Woodlark) and the third, a control group had served in New Guinea, where manifestations of filariasis in American troops have been slight, or had had no tropical service. These same cases have already been the subject of extensive reports by HODGE, DENHOFF and VANDER VEER [this *Bulletin*, 1945, v. 42, 1020] and by BEHM and HAYMAN [this *Bulletin*, 1946, v. 43, 762]. The present account does not materially add to the information already published and should be consulted in the original, in conjunction with the other papers, by those interested.

A. R. D. Adams.

OLIVEIRA, E. de S. Elefantíase e estados elefantinos. (Notas de Cirurgia—Bahia, 1941.) [**Elephantiasis and Elephantoid Conditions.**] *An. Facul. de Med. Bahia.* 1944–45, v. 4, 111–51, 45 figs. [17 refs.]

The author gives details of the history and of the general clinical state and the local conditions of 9 cases of elephantiasis, three each of the foot and leg, the scrotum, and the vulva. This is followed by a brief consideration of other growths with which elephantiasis might be confused, for example hypertrophy of the breast, molluscum, tumours of the testicle, large hernias, even rhinophyma. Finally, line drawings show the steps of operative treatment. The paper is almost entirely a surgical one. The illustrations are clear.

H. Harold Scott.

HAWKING, F. & BURROUGHS, Ann M. **Transmission of *Litomosoides carinii* to Mice and Hamsters.** [Correspondence.] *Nature.* 1946, July 20; 98.

KUITUNEN-EKBAUM, E. **Phenothiazine in the Treatment of Enterobiasis (II).** *Canadian J. Pub. Health.* 1946, Mar., v. 37, No. 3, 103–13. [22 refs.]

Phenothiazine was given to 1,275 subjects (900 children and 375 adults) infested with *Enterobius vermicularis* and the results of this treatment were estimated by means of the N.I.H. swab. Before and after the treatment the blood haemoglobin of 25 children and 9 adults was estimated.

The ages of the subjects, who came from all social levels, ranged from three months to 78 years. Eleven children were less than 1 year old and 8 adults were 60 years old or older. Those under 15 years old are called children, those over 15 years are called adults. Before treatment NIH swabs were taken on five consecutive mornings ; if eggs of *E. vermicularis* were found, treatment was given. During the second week after the end of treatment, 7 NIH swabs were taken on five consecutive mornings. When the first course of treatment was not effective, treatment was repeated four weeks later. Diagnostic swabs were taken from 2,505 subjects (1,380 children and 1,125 adults) and phenothiazine was given to 1,275 (900 children and 375 adults). Post-treatment swabs were taken from 790 (584 children and 206 adults) and the results given are based on these.

The phenothiazine used was supplied by the Connaught Laboratories and was refined and made into 0·5 gm. tablets by SIEBENMANN [see SCHNITZER, SIEBENMANN and BETT, this *Bulletin*, 1942, v. 39, 862]. The author emphasizes the necessity of using highly purified phenothiazine.

Two dosage scales were tried. Scale A was 2·5 to 9 gm. for children in proportion to their age, and 9 gm. for adults, given over four to six days ; this scale caused toxic reactions, especially in small children and it was abandoned. Scale B was therefore used, and was given over a period of 4 days. This scale was as follows :—

Under 2 years	0·25 gm. per day,	total 1 gm.
2 to 3 years	0·5 gm. ,, ,,	,, 2 gm.
4 to 5 years	0·75 gm. ,, ,,	,, 3 gm.
6 to 7 years	1·0 gm. ,, ,,	,, 4 gm.
8 to 9 years	1·25 gm. ,, ,,	,, 5 gm.
10 to 11 years	1·5 gm. ,, ,,	,, 6 gm.
12 to adult of over 15 years	1·75 gm. ,, ,,	,, 7 gm.

For small children the tablets were crushed and mixed with food or orange juice ; other subjects were advised to chew and swallow the tablets. Extra fluid and avoidance of constipation were advised during treatment. Tables show the results of treatment.

Dosage scale B was given to 584 persons (408 children aged 7 months to 15 years and 176 adults over 15 years). The swabs of 327 (80·2 per cent.) of the 408 children were negative after the first course of treatment, those of 76 children (18·6 per cent.) after the second course and 5 (1·2 per cent.) children needed a third course. Of the 176 adults, 150 (85·2 per cent.) gave negative swabs after the first course, 20 (11·4 per cent.) gave them after a second course and 6 (3·4 per cent.) needed a third course.

The toxic reactions are discussed in detail under the following headings :—

Anaemia.—Reduction of the haemoglobin level was the commonest evidence of this, and was sometimes so severe that emergency treatment was required. The case histories of three girls, aged 18 months, 8 years and 2 years respectively, are given to illustrate this form of toxic reaction. Blood transfusions were given successfully to all three. The haemoglobin values of 25 children and 9 adults were estimated ; all were given the dosage scale B, the first estimation being done before the first dose and the second on the fifth day after the last dose. The results showed that two children had a decrease of 3 gm. per 100 cc. of blood, four a decrease of less than 2 gm., 13 a decrease of less than 1 gm., while two showed no change and two showed slight increase. Of the nine adults tested, two showed a decrease of more than 2 gm., one a decrease of 1 to 2 gm., four a decrease of less than 1 gm. and two showed no change. The author refers to the work of MILLER and ALLEN [this *Bulletin*, 1942, v. 39, 781] and of BERCOVITZ *et al.* [this *Bulletin*, 1943, v. 40, 929] who also found anaemia after administration of phenothiazine.

Skin Reactions.—These were neither serious nor common. They included skin rashes, pruritus and oedema.

Fever.—Other authors have reported a rise of temperature during treatment with phenothiazine. The present author reports a temperature of 100°F. in a girl aged 6 years after one dose of phenothiazine, and a temperature of 102°F. in an adult female after one dose of 1·75 gm. ; treatment of both these subjects was discontinued.

Miscellaneous reactions were slight pain in the abdomen in two children ; several mothers reported pallor and decline of appetite during treatment of children. The author points out that various workers have used very variable doses of phenothiazine, and he claims that all the serious toxic reactions reported in the literature have occurred after doses above his dosage scale B, although sometimes large doses have had no ill effect. Thus, MANSON-BAHR [this *Bulletin*, 1941, v. 38, 516] gave 7 to 40 gm., and ELLIOTT [this *Bulletin*, 1943, v. 40, 702] gave 24 gm. Both these authors, however, gave a laxative with the phenothiazine and may thus have avoided toxic reactions. Some of the toxic reactions experienced by the present author were, he thinks, related to previous ill health, and it would have been wiser to have reduced the dose and to have repeated it if necessary, or to have waited until the health improved. [It would appear wise to raise the haemoglobin level, especially, before phenothiazine is given.]

Discussing precautions that should be taken, the author says that phenothiazine is more toxic than gentian violet but is more effective, and is apparently tolerated by a larger number of individuals than gentian violet ; it also requires a shorter period of treatment and is easily given to small children who cannot swallow gentian violet tablets. The phenothiazine must be highly purified, the patient should be in fair general health, constipation during treatment should be avoided, the drug should be discontinued at once if toxic reactions appear and it should not be repeated before 3 to 4 weeks after the first course. Pregnancy and lactation seem to be no bar to its use, but supervision of such patients is necessary. Discussing the treatment of families with phenothiazine,

the author says that swabs have shown that, usually, if one member of the family is infected, so are the other members; it is therefore futile to treat only one or some of them. Even if more than five swabs are taken, slight infestations may be missed, for one boy aged four years gave five negative swabs, yet the mother later sent a specimen of *Enterobius* which had been passed. [See also SCHÜFFNER and SWELLENGREBEL, this *Bulletin*, 1945, v. 42, 924, who consider that their method is better than the NIH swab for detection of light infestations, and SCHÜFFNER, *ibid*, 1946, v. 43, 233. DAVEY & INNES (this *Bulletin*, 1942, v. 39, 861) also review the toxicity of phenothiazine. SISK (this *Bulletin*, 1943, v. 40, 927) gives other dosage scales.]

G. Lapage.

DEFICIENCY DISEASES.

CULLINAN, E. R., KEKWICK, A., WATTS, A. S. & TITMAN, W. L. **Description of an Outbreak of Beriberi with special reference to the Aetiology of Beriberi and Epidemic Dropsy.** *Quarterly J. of Med.* 1946, Apr., v. 15, No. 58, 91–105, 2 figs. on 1 pl. [26 refs.]

There exists amongst populations, whose staple food is rice, a clinical pattern for which aetiological factors have been found. Of the known factors, lack of thiamin, producing beriberi, and a toxin, producing epidemic dropsy, are the most important. This paper concerns an outbreak of the syndrome amongst troops, in which it was possible to trace in detail the sources and issues of the various articles of food.

The troops formed part of the East African forces located in an isolated garrison town [presumably in Mauritius]. They were composed of British, Africans and Mauritians. All were housed in good barracks and were living under excellent conditions. The climate was hot and humid, but did not differ materially from that experienced during previous years. The outbreak started suddenly on March 12, 1945, when nine men reported sick with oedema of legs; eventually 59 cases were found, all in East Africans, making an incidence of 38 per 1,000.

Twenty-two patients were examined in hospital. All had oedema of legs; in many this was followed by a feeling of tightness of the legs on walking, and in some of pain; in two cases the gait was markedly affected. Their general physical state was rather better than in a large group of East African soldiers examined elsewhere.

Peripheral neuritis was evidenced by sluggish or absent deep reflexes in 18 cases, and by diminution of sensation to light touch or superficial pain in 16; deep sensation was unaffected. No clinical evidence of enlargement of the heart was discovered, but teleradiograms revealed right-sided dilatation in four of eight examined. Electrocardiograms were taken of nine; right ventricular preponderance was shown in three, and shortening of the P/R interval was present in almost all.

The adrenaline test proved negative in all 22 cases and no drop in the diastolic pressure was recorded. The capillary fragility test was also normal. The most interesting feature was the plasma-proteins. In East African soldiers on standard army diet the proteins are normal in range, but there is a reduction of the albumin-globulin ratio; in the present series the albumin-globulin ratio was raised rather than lowered, but no explanation of this fact was found.

Treatment was given to 63 cases, under controlled conditions. To the first group 1 mgm. of thiamin and 1 oz. of yeast daily; to the second 1 oz. of yeast;

and to the third a small dose of ammonium chloride as a control. The duration of the disease was shortened in the first group; the second was intermediate between the first and third in this respect.

The oedema of the legs, the right-sided cardiac dilatation and the peripheral neuritis supported the diagnosis of a beriberi-like syndrome. As regards the clinical differentiation between beriberi and epidemic dropsy, the absence of haemorrhages, the normal capillary fragility and the absence of gastro-intestinal symptoms are in favour of the former.

Diet.—The staple article of food in the diet of East African troops was maize-meal, but in November 1944 it was found that the isolated position of the garrison and climatic conditions precluded its use. Nineteen ounces of rice were therefore substituted for previous issues of 16 oz. of maize meal and 4 oz. of rice. By the middle of February, and just previous to the outbreak, the diet of African troops was considerably changed, because the beans were unfit to eat, and fresh vegetables were scarce. The European and Mauritian troops were on different scales of diet, and their food was considerably more varied than that of the Africans. Rice formed a much greater proportion of the African diet in relation to known food factors and bulk; moreover, the relation of first to second class protein was better in the European and Mauritian diets. The rice was lightly milled and contained 0·03 mgm. of thiamin per oz., but mycological examination revealed that 0·4 per cent. of its weight was made up of contamination with spores and sporangiophores of a mucor. This is a surface contamination which can be removed by washing, but considerable difference was found in the attention paid to the cleansing and care of the rice. The total theoretical intake of thiamin by the three races differed little; if anything that of the Africans was higher than that of the Mauritians, yet the outbreak was confined to the former, and by most observers the total thiamin intake would be considered adequate (0·49–1·09 mgm. daily, or from 0·25–0·55 mgm. per 1,000 calories). When tested on pigeons the thiamin was found active and adequate.

As lack of thiamin was apparently not the cause of the outbreak, the alternative theory of a toxin was examined. The possibility of a water-borne contamination was discarded. Epidemiological evidence suggested that the toxin acted upon the thiamin rather than upon the subject.

From carefully controlled experiments it was shown that the destruction of thiamin in contaminated rice was much greater than in fresh rice cooked in the same way, for the same time and in the same pans.

The amount of heat acting on the rice appeared also to increase the amount of destruction. Confirmation of this was obtained by estimating samples taken from the top and bottom of the pan; the destruction was 58 per cent. at the top and 86 per cent. at the bottom. Thirdly the time for which the rice was cooked affected the amount of destruction. Confirmation of the theory of destruction of thiamin by cooking was provided by pigeon experiments. When four birds, which had previously been nourished on 0·8 oz. of uncooked suspected rice *per diem*, were fed on the same dry weight cooked, they disclosed signs of thiamin deficiency, even more rapidly than those on polished rice.

The opinion was formed that, whilst the thiamin rice content was adequate to prevent beriberi, some other substance had developed in the rice, during the process of cooking, which destroyed it, so that the cooked grain produced beriberi.

The final conclusion is to the effect that outbreaks of epidemic dropsy should be regarded as beriberi until it can be shown that the thiamin is not destroyed in the process of cooking, and that it is of little value to estimate the thiamin content of uncooked rice and to calculate therefrom the supposed thiamin intake.

It is possible that thiamin lack is the one aetiological factor which accounts for both these diseases. At first it seemed a typical outbreak of beriberi, although the explosive character suggested that it might be epidemic dropsy.

Philip Manson-Bahr.

PROC. ROY. SOC. MED. 1946, May, v. 39, No. 7, 357–60 (Sect. of Med. 9–12).
Discussion : Nutritional Neuropathy in Repatriated Prisoners of War from the Far East [CLARKE, C. A. & SNEDDON, I. B. ; CULLINAN, E. R. ; SPILLANE, J. D. ; KIRMAN, B. D.].

Drs. Clarke and Sneddon reported some of the neurological signs found in men who had been released from Hong Kong [see *Bulletin of Hygiene*, 1946, v. 21, 527]. Some patients developed fresh neurological signs in hospital while eating a full diet supplemented by adequate amounts of thiamin parenterally. This fact was part of the evidence put forward by them in support of the theory that the neuropathy was not caused by simple lack of the vitamin B complex. In their opinion the syndrome was due to an anti-vitamin or toxic factor present in the rice that inactivated what little thiamin was present in the diet. The thiamin deficiency was rendered more severe by the low protein intake that prevented adequate synthesis by bacteria in the gut. Changes in the nervous system appeared to be irreversible.

Dr. Cullinan described an outbreak of beriberi amongst East African troops whose diet consisted largely of lightly milled rice, which in its uncooked state contained theoretically adequate amounts of thiamin. It was found that the rice, which was old and showed surface contamination with a variety of mucor, lost over 70 per cent. of its thiamin during cooking, whereas similar freshly milled rice lost only 30 per cent. [See also CULLINAN *et al.* above.]

Dr. Spillane summarized the clinical features of the nutritional neuropathic syndromes he had observed in prisoners of war during the past few years.

Dr. Kirman reported that there was no increase in the incidence of psychosis amongst released prisoners who passed through India, and none of the few psychotics seen showed signs of pellagra.

H. E. Harding.

SIMPSON, J. **" Burning Feet " in British Prisoners-of-War in the Far East.** *Lancet.* 1946, June 29, 959–61.

Large bodies of Allied troops in Java capitulated to the Japanese in March 1942. Signs of deficiency disease, which soon affected half of the prisoners, developed after four months, showing first as lesions of the mouth and scrotum. Shortly after these signs of pellagra and ariboflavinosis had become manifest on a large scale, a few men began to report sick with " burning feet ", and during the following 3 months, 10–12 per cent. of the prisoners had this complaint.

Most of the sufferers showed exaggerated knee and ankle jerks, but no ankle clonus nor extensor plantar response, and no spasticity. Early hyperaesthesia in the feet and lower legs was usually replaced by hypoaesthesia ; both sensory alterations showed a patchy distribution. No ataxia, incoordination or loss of joint sense was demonstrated. The condition commonly became so severe as to dominate the life of the sufferers. Treatment with vitamin A ($\frac{1}{2}$ oz. red palm oil daily for 4–6 weeks) produced no improvement : 10 patients given 10 mgm. thiamin daily for a month showed no benefit. Giving the kachang hijau bean (*Phaseolus radiata*) in doses of 150 gm. daily cured the syndrome in 4–6 weeks. This bean is reported to be a rich source of vitamins B_1 and B_2 ; in other camps the syndrome was cured by yeast or marmite.

Associated with burning feet, but appearing a little later, local eye irritation developed, followed closely by blurring of the vision and loss of visual acuity. After a rapid onset the visual upset usually remained stationary or tended to

improve very slowly. About 10 per cent. of those with burning feet developed retrobulbar neuritis; visual defects occasionally developed without the peripheral pains, but the two conditions were usually associated. Cure of the "burning feet" syndrome did not affect the visual condition.

H. E. Harding.

HARRISON, G. F. **Nutritional Deficiency, Painful Feet, High Blood-Pressure in Hong-Kong.** *Lancet.* 1946, June 29, 961–4, 1 fig.

Although many other conditions were met with in prisoners-of-war in Hong Kong, the outstanding symptom almost throughout the Japanese occupation was painful feet. In the early days the pain was so severe that the only drug that gave relief was morphine in ½ grain doses by mouth. Later, the intensity of the pain diminished, and less potent drugs were effective. The pains were accompanied by lost or diminished sensitivity to touch, pin-prick, heat and cold, and often by loss of joint sense and sense of position in the toes.

Eleven patients were given 10 ml. of 10 per cent. calcium gluconate intravenously on several occasions. They appreciated a "flush" spreading down the body, and if this sense of warmth reached the feet the pain was sometimes relieved for a time. Some of the patients who were given 20 mgm. nicotinic acid subcutaneously or 100 mgm. by mouth obtained relief from pain, and one patient experienced almost immediate complete relief for about 5 minutes after inhaling the contents of one ampoule of amyl nitrite. Exercise had a beneficial effect on the pain, and those who conscientiously walked as much as possible each day made a speedier recovery than those who could not or would not make the effort. Recovery took years rather than months, despite daily doses of 20 mgm. nicotinic acid subcutaneously, 3–5 mgm. thiamin chloride by mouth, yeast drinks and other foods containing vitamin B complex. [Much of this is contrary to the findings of Simpson—see above.]

At least 19 per cent. of the 400 patients suffering from malnutrition had at some time—usually at an early stage—a high diastolic blood pressure. In many of these the systolic pressure was also raised. In a few patients simultaneous records were made each week of the blood pressure in arm and leg. Almost always the systolic pressure was higher in the leg than in the arm, and in one instance was 50 mm. Hg higher. Not all patients with a raised blood pressure had pain.

The author suggests that the cause of the pain and of the high diastolic pressure was spasm of the blood vessels in the legs. *H. E. Harding.*

BLANKENHORN, M. A., VILTER, C. F., SCHEINKER, I. M. & AUSTIN, R. S. **Occidental Beriberi Heart Disease.** *J. Amer. Med. Ass.* 1946, June 29, v. 131, No. 9, 717–26, 1 fig. [Refs. in footnotes.]

Heart disease as a manifestation of beriberi was recognized in 12 patients admitted to the Cincinnati General Hospital from 1940 to 1945. All the patients were chronic addicts to alcohol, but this substance is not considered to be a direct cause of the condition. The ages of the patients ranged from 33 to 67 years, and only one was a woman. Five patients died in hospital, and one died 3 months after being discharged. Two patients recovered with rest in bed, a full diet, and digitalis: one of these died 3 months later. The response to large doses of thiamin was rapid in only one patient, the others recovered slowly.

The authors think that the criteria for diagnosis of the condition have been set too high, and propose the following as aids to its recognition: (1) insufficient evidence of other aetiology; (2) a diet deficient in thiamin for at least three months; (3) signs of neuritis or of pellagra; (4) enlargement of the heart with sinus rhythm; (5) dependent oedema; (6) a raised venous blood pressure;

(7) minor changes in the electrocardiograph ; (8) recovery with decrease in the size of the heart, or post-mortem findings consistent with beriberi.

Three autopsies were performed. One subject showed dilatation of both ventricles, the other two had hypertrophy as well as dilatation. All showed degenerative changes in heart muscle fibres and "interstitial oedema". The nervous system of two subjects was examined : both showed degenerative changes in the cells of the nucleus sympathicus and of the tracts of the lateral horn in the upper cervical segments of the spinal cord, damage of spinal cord roots, and far advanced degeneration of the vagi and some of the peripheral nerve trunks. The significance of these lesions of the central nervous system in the pathogenesis of the heart disorder is uncertain. *H. E. Harding.*

SPRUE.

Cooke, W. T., Elkes, J. T., Frazer, A. C., Parkes, J. & Peeney, A. L. P. **Anomalies of Intestinal Absorption of Fat. I. The Determination and Significance of Faecal Fat.** *Quarterly J. of Med.* 1946, Apr., v. 15, No. 58, 141–55. [59 refs.]

Two main theories have been formulated to explain normal fat absorption from the intestine. The lipolytic hypothesis of Verzar and McDougall, 1936, suggests that fat must be completely hydrolysed and that the resultant fatty acid passes into the cells in combination with bile salts. In the cell triglyceride is resynthesized after phosphorylation under the control of the adrenal cortex. The re-formed fat then passes entirely by the thoracic duct into the systemic circulation. The "partition hypothesis" (Frazer 1938) suggests that fat is only partly hydrolysed. The unhydrolysed portion is finely emulsified by a monoglyceride-bile-salt-fatty-acid complex and this enters the intestinal cell as a finely dispersed emulsion. Some of the fat is absorbed as fatty acid. The unhydrolysed fraction passes mainly by the thoracic duct to the systemic circulation and the fat depots, whereas most of the fatty acid passes direct to the liver *via* the portal vein. Phosphorylation may play a part in the modification of the interfacial film of the unhydrolysed fat globules. The effect of the adrenal cortex is possibly secondary to its influence on electrolyte metabolism.

In view of the differences of opinion on the normal processes of fat absorption it is small wonder that the pathology of anomalous fat absorption still remains obscure.

Methods.—A standard diet containing 50 gm. fat, 250 gm. carbohydrate and 75 gm. of protein was used. The food equivalents were calculated from standard food tables and checked from time to time. The patient was placed on this diet 48 hours prior to the commencement of the test. The use of a 50 gm. fat intake as the standard, whilst well tolerated by patients with steatorrhoea, proved to have certain disadvantages. The production of a palatable fat-free diet is a difficult matter.

In the collection of specimens two methods were used.

In the first, three capsules of carmine (0·9 gm.) were given on an empty stomach at 7 a.m. on the first day of the test and at the same hour two, three or four days later, charcoal (2 oz.) in water was given. The stools were examined as passed and saved as soon as the carmine appeared ; the first containing charcoal was discarded and collection completed.

The second method entailed the administration of 500 cc. of normal saline as an enema after the evening meal. The result was discarded. A second saline enema was given two, three, or four days later at the same hour. The results of this, together with the stools passed after the first enema, completed the

collection. This proved eventually to be the most convenient. The period of collection was 48 hours with fluid or semifluid faeces, and 72 or 96 hours in the case of patients with normal or constipated stools.

Methods of analysis.—Five-sixths of determinations were made by Cammidge's (1913) modification of the Schmidt-Werner method: the remainder by a wet extraction method.

Selection of patients.—Three groups of patients were used as controls. In the first (15) the only criterion for inclusion was the presence of diarrhoea; in three charcoal appeared in less than seven hours after administration. In none was there any evidence of steatorrhoea. The diagnoses included ulcerative colitis, amoebic dysentery, gastro-enteritis and chronic anxiety states. The second group of 12 was under treatment for anaemia. The third group of 14 cases consisted of hospital patients chosen at random.

In 79 other patients an excess of faecal fat might have been expected, or was demonstrated. These included 29 cases of idiopathic steatorrhoea; 21 of tropical sprue, five of which were seen in relapse and had been under treatment for 3–10 years. Eight had been diagnosed in India on account of anaemia, glossitis and diarrhoea with high percentage of faecal fat, but had made a complete recovery. The remaining eight cases still had some fat intolerance and minor biochemical changes; 7 of pancreatitis (the diagnosis in five was confirmed by autopsy or operation); two of lacteal obstruction; six of surgical conditions (gastrocolic fistulae, ileotransverse colostomies and Crohn's disease with ileal resection); six of malnutrition in repatriated prisoners of war; and a miscellaneous group of eight (four of which had duodenal ulceration in addition to long-standing steatorrhoea).

Results.—The results of 160 observations in 120 patients are summarized in tables.

In 41 control patients, more than 95 per cent. was usually absorbed, with variations between 91 and 99 per cent. In 29 cases of idiopathic steatorrhoea the average absorption was 73 per cent. (range 29 to 91). In pancreatitis the absorption varied from 18 to 91, the daily excretion from 4·6 to 40·9 gm., and in six the free fatty acids exceeded the neutral fats. In malnutrition two showed minor defects of absorption.

Microscopic examination of faeces of idiopathic steatorrhoea and tropical sprue usually showed an excess of fatty acid crystals. Whilst the presence of excess of fatty acid frequently indicates steatorrhoea, there were a sufficient number of exceptions to render this qualitative method of diagnosis unreliable.

The amount of fat in faeces can be determined by analysis of a single specimen or of a cumulative specimen collected over a known period. If the first method is used the result can be expressed only as a percentage of the faecal dry weight and the result interpreted in relation to more or less arbitrary normal limits. Great variation in faecal dried weight occurs with different or similar diets, depending on the amount of the unabsorbed residue. Even when careful dietary control is exercised, great variation in the non-fatty residue may change the fat percentage from abnormal to normal levels, or *vice versa*. Phasic variations in absorption are not uncommon, making the examination of only one small sample of faeces undesirable. In addition the normal physiological range has not been satisfactorily agreed upon; various authors give it as ranging from 15 to 50 per cent.

The estimation of non-dietary fraction of faecal fat as a routine procedure in patients is difficult and there is little evidence to indicate that this fraction was disproportionately increased in any of the cases under investigation.

The response of these patients to a low fat diet and the presence of associated signs of defective absorption support the view that excess of faecal fat is derived from unabsorbed material.

Percentage absorption figures were calculated directly from the difference between the amount of fat ingested and that found in the faeces over the comparable period. When the percentage absorption is calculated in this manner, it was found to be 95 or over in the controls. In practice it was found that cases with percentage absorption of less than 85 invariably showed associated signs and symptoms confirming a fat-absorption defect.

Seventy to eighty per cent. of faecal fat is normally present as fatty acid or soap. The degree of splitting of neutral fat is interpreted as an index of pancreatic function, but this is not invariably so, because even after complete pancreatectomy in man lipolysis still occurs, for lipase exists in the gastric and intestinal juices. The percentage hydrolysis of fat in the faeces cannot therefore be regarded as a reliable index of normal pancreatic function.

The interpretation of changes in the chemical characteristics of faecal fat is at present unsatisfactory. The authors were unable to demonstrate any constant features in the faecal fat in their series. Usually about half the split fat is present as soap, although considerable variations are found in case to case.

It has been suggested that the rapid rate of passage of intestinal contents through the alimentary tract might constitute an important factor in the production of a fault in fat absorption. In those cases of diarrhoea in which charcoal passed through the alimentary tract within seven hours of ingestion, fat absorption was normal. It is therefore concluded that, when intestinal hurry can be demonstrated in these cases, the colon is primarily involved and consequently defective absorption of fat cannot be attributed to lack of time.

In addition to the investigation of the amount of fat in the faeces, the absorption of fat may also be investigated by examination of the blood during the post-absorption period either by chemical analysis or by chylomicrograph. In the normal subject a characteristic lipaemia can be demonstrated in the systemic blood during four hours after ingestion of fat, and it was a striking feature of many of the cases of defective fat absorption that whilst fat balance tests indicated that 70–80 per cent. absorption had occurred, there was little or no change in the blood-fat.

The constantly flat chylomicrograph curve and correspondingly low value for blood-fat obtained in chemical analysis are difficult to explain, unless it is assumed that the fat is leaving the intestine by some pathway other than the thoracic duct and systemic blood. *P. Manson-Bahr.*

KARAMCHANDANI, P. V. & HYDER, G. **Analysis of 242 Cases of Sprue in Indian Troops.** *Indian Med. Gaz.* 1946, Jan., v. 81, No. 1, 11–13.

" Para-sprue " corresponds to what has so far been known as " incomplete sprue ", " chronic jejuno-ileal insufficiency ", or a vitamin B deficiency syndrome allied to sprue.

The authors' view of the pathological process is as follows :—With faulty intake and faulty absorption, the stress initially falls on the delicate columnar intestinal epithelium, and the symptoms evoked depend upon the site and extent of the damage. When the duodeno-jejunal region is attacked, there may be deficiency of bile flow, failure of emulsification, and increase of split fat in the stools, because it cannot be absorbed ; or there may be deficiency of pancreatic secretion resulting in high total fat content in the stools. When the ileum is affected, the fat content in the stools is normal, and the diarrhoea is of the irritative type (enteritis), but when the colon is involved blood and mucus may appear in the evacuations.

The post-mortem appearances in two typical cases are recorded. The small intestine is described as wasted, with destruction of villi and desquamation of the epithelium.

A series of 242 cases of the sprue syndrome was observed during a period of 2½ years. These were grouped as follows :—dyspepsia and diarrhoea 88 ; dyspepsia, diarrhoea and glossitis 96 ; the same signs with addition of anaemia 54 ; the same with excessive split fat in the stools 4.

The majority of cases fell within the age-group 20–25 ; the duration of the disease bore no relation to its severity. Thirty-one cases had associated amoebic infection, but six only had blood and mucus in the stools.

Treatment at first consisted of 8 oz. of milk given every 2 hours from 6 a.m. to 10 p.m. This was increased to 10 oz. during the next 4 days. This diet provided a Calorie value of 1,625, with 82 gm. protein, 90 gm. fat and 120 gm. carbohydrate. During the second and third weeks additions were made to the diet, which was increased to 2,560 Calories with 97, 70 and 458 gm. of protein, fat and carbohydrate respectively. During the next three weeks it was augmented to 3,200 Calories with 154,114 and 596 gm. protein, fat and carbohydrate respectively. Vitamin-containing foods, fruit juices, and liver preparation were given.

Those with concomitant amoebic infection were given routine treatment by emetine, Yatren, emetine bismuth iodide and Amoebiarson.

Of the 242 cases 129 were cured and discharged to duty ; 22 were improved and placed permanently in category C ; 67 were improved, placed in category C, but relapsed ; 22 were not improved, and were invalided out of the service. Two patients died. *P. Manson-Bahr.*

SPIES, T. D., FROMMEYER, W. B., GARCIA LOPEZ, G., LOPEZ TOCA, R. & GWINNER, Georgia. **Haemopoietic Action of 5-Methyl Uracil (Thymine) in Tropical Sprue.** *Lancet.* 1946, June 15, 883–5, 2 figs.

Since synthetic 5-methyl uracil (thymine) produces a striking haematological response in Addisonian pernicious anaemia in relapse, and as the bone marrow of this condition is indistinguishable from that associated with the macrocytic anaemia of tropical sprue, four patients suffering from relapse of the latter disease were given 7·5 gm. of the drug twice daily by mouth for 9 to 16 days. In each case there was a definite haematological response, parallel to, although less dramatic than, that which follows the administration of synthetic folic acid. Reticulocytosis began on the fourth or fifth day, reaching a peak on the eighth or ninth day, of treatment, and was followed by an increase in the erythrocytes and haemoglobin. On the day after the peak reticulocytosis, the bone marrow consisted largely of normoblasts with almost complete obliteration of the megaloblastic arrest found before treatment. Clinical improvement was manifested by an increase in appetite and strength, resolution of the glossitis, and disappearance of the burning and soreness of the tongue and mouth. Although the stools did not become fully formed, they showed, as early as the fourth day of treatment in one case, a return towards normal. X-ray examination of the gastro-intestinal tract showed a substantial decrease in intestinal motility, in spasm and dilatation, and in the amount of "puddling" of barium, after administration of the drug. Glucose-tolerance tests indicated that intestinal absorption improved after therapy.

F. Murgatroyd.

DARBY, W. J. & JONES, E. **Treatment of Sprue with Synthetic *L. casei* Factor (Folic Acid, Vitamin M).** *Proc. Soc. Exper. Biol. & Med.* 1945, Nov., v. 60, No. 2, 259–60.

This is a report of the first two of the three cases of sprue treated with synthetic *L. casei* factor which were recorded by DARBY, JONES and JOHNSON

[this *Bulletin*, 1946, v. 43, 667] ; the authors state that " there appears to have been published no previous experiences with this factor in the treatment of sprue." *J. F. Corson.*

CARRUTHERS, L. B. **Chronic Diarrhoea treated with Folic Acid.** *Lancet.* 1946, June 8, 849–50.

Four severe cases of hypochromic anaemia were treated with 40 to 60 mgm. folic acid daily for five to seven days without any noteworthy improvement in the anaemia, but in two of the patients who had chronic diarrhoea an immediate and definite improvement in the stools occurred. This led the author to try the effect of folic acid on six other cases of chronic diarrhoea of vaguely determined aetiology. In these cases the stools became normal, or approximately so, within two to five days of starting the treatment. He therefore suggests that in any long-standing diarrhoea a nutritional factor prolongs the production of abnormal stools, and that folic acid appears to correct this defect.

F. Murgatroyd.

JENSENIUS, H. **Results of Experimental Resections of the Small Intestine on Dogs. (Experimental Enteroprival Sprue.)**

This book is reviewed on p. 971.

HAEMATOLOGY.

ZUELZER, W. W. & OGDEN, Faith N. **Megaloblastic Anemia in Infancy. A Common Syndrome responding specifically to Folic Acid Therapy.** *Amer. J. Dis. Children.* 1946, Mar., v. 71, No. 3, 211–43, 7 figs. (1 coloured on 1 pl.) [Refs. in footnotes.]

Macrocytic anaemia commonly occurs in infancy as a result of a specific dysplasia and dysfunction of the bone marrow developing in the absence of an essential haematopoietic principle. Clinically the outstanding feature is extreme pallor, with weakness, loss of appetite and irritability ; fever, vomiting and diarrhoea are common complaints. In the series of the 25 patients studied, many of the infants had cough, coryza or both for several weeks before admission to hospital, and the beginning of the illness was usually referred to the onset of these symptoms. In several cases petechiae had been noted by the parents. On examination, a soft systolic murmur could often be heard over the praecordium, and slight cardiac enlargement was evident. The liver was invariably increased in size, but the spleen was palpable in only 10 of the patients. In no case was there any appreciable lymphadenopathy. Half the patients were underweight, six had clinical signs of scurvy, and 19 had fever of variable degree.

The disturbance in erythropoiesis was shown in the bone marrow by the prevalence of young basophilic and polychromatic cells, limitation of mitotic activity, abnormal karyokinesis, an abnormal nuclear structure, lobulation and distortion of the shape of the nuclei, an increased tendency to denucleation, and an increase in the size of the cells and in the relative amount of cytoplasm at all levels of maturation. The pattern corresponded basically to that seen in pernicious anaemia in relapse, and was typical of alterations produced by lack of a so-called maturation factor, resulting in multiplication of cells confined mainly to primitive levels. Similarly leucopoiesis showed constant qualitative changes leading to a relative decrease in the number of mature cells.

The peripheral blood showed always a severe anaemia, with haemoglobin levels near 5 gm. per 100 cc., and often below 3 gm. Reduction of the red blood cells was often even more pronounced, and the colour index was usually, but not invariably, well above unity. The mature erythrocytes appeared well filled with haemoglobin, and this was borne out by the mean corpuscular haemoglobin concentration. Polychromasia and punctate basophilia were invariably present to a slight degree, and Howell-Jolly bodies and Cabot rings were often seen. The percentage of reticulocytes was usually small, and obviously did not account for the macrocytosis of the blood. Nucleated red cells were always found, but sometimes only after prolonged search. The white cell count was below 10,000 per cmm. in most cases, despite the presence of fever or other signs pointing to infection, and in some cases a frank leucopenia existed. Neutropenia was common, being as a rule moderate but sometimes pronounced. The neutrophils were usually much larger than normal, being of two basic types, with transitions between the extremes. The first was characterized by excessively large nuclei of the metamyelocyte type, often showing budding, twisting and the beginning of segmentation, while the granulation of the cytoplasm was uneven and suggested immaturity. The second type showed fully developed granulations of the cytoplasm, and excessive segmentation of the nuclei, with long tenuous filaments connecting the lobules. The platelets were reduced in number, often markedly, and the thrombocytopenia accounted for the prolonged bleeding time, inadequate clot retraction, and the haemorrhagic manifestations shown by several of the patients.

Infections and other complications were common, and multiple transfusions were often necessary. These factors limited the number of cases suitable for the evaluation of specific therapy to 12. In these latter, the effect of crude or purified liver extract given parenterally, and that of folic acid, appeared to be identical, whether the folic acid was given orally or parenterally in the form of concentrates or as synthetic material. A second reticulocyte response could not be produced by liver extract when folic acid had been given first, and *vice versa*. Since liver contains folic acid, the identity of the therapeutic effect raises the question whether, for this form of anaemia, liver extract owes its efficacy to its folic acid content. Between the third and fourth day after beginning treatment with folic acid, in dosage of from 5 to 100 mgm. daily, the reticulocytes in the blood began to rise, and shortly afterwards the haemoglobin level and the red blood cell count began to improve. The reticulocytes usually reached a considerable peak in another three to four days and then decreased rapidly, while the haemoglobin level and the red cell count continued to rise. The neutrophil leucocytes also increased and the hypersegmented forms gave way to normal cells within seven to sixteen days ; sometimes a slight eosinophilia appeared. The platelets also increased in number soon after therapy was started. The bone marrow underwent a striking transformation and assumed a normal pattern within a few days. Unless other illnesses interfered, the patient's appetite rapidly improved, the colour returned and the irritability disappeared. Splenomegaly and hepatomegaly, although often persisting for some weeks after treatment, eventually disappeared. In a follow-up period ranging from 3 to 20 months, there were no recurrences of this type of anaemia in any of the patients who did not succumb to complications.

Inadequate diet and probably conditions interfering with proper absorption in the intestinal tract are possible factors producing the deficiency leading to this anaemia of infancy, but it seems doubtful that these are the only factors concerned, while the frequency of infections was striking. It is suggested that infections and nutritional deficiencies are aetiologically significant, while race, age and possibly prematurity and maternal anaemia are predisposing factors.

F. Murgatroyd.

ZUELZER, W. W. **Folic Acid Therapy in the Anemias of Infancy and Childhood.** *J. Amer. Med. Ass.* 1946, May 4, v. 131, No. 1, 7–8, 1 chart.

This paper is another report on the effect of folic acid on the anaemia with a megaloblastic type of blood formation in the bone marrow, which is not uncommon in white infants under the age of 18 months. [See ZUELZER & OGDEN, above.] The characters of this anaemia are as follows. There is a severe normochromic anaemia, usually, but not invariably with macrocytosis; there is a tendency toward leucopenia and neutropenia, with giant metamyelocytes, macropolycytes and hypersegmented neutrophils in the peripheral blood; the platelets are diminished, sometimes to a severe degree, and there is an increased tendency to bleeding; and the bone marrow is frankly megaloblastic, resembling that of pernicious anaemia in relapse. Splenomegaly is common, but not constant; some infection is usually present; the nutritional history is usually poor; and histamine-fast achlorhydria is often present although it does not persist after the anaemia is cured.

Twelve patients suffering from such an anaemia were treated with folic acid in synthetic form, or by oral administration of concentrates rich in *Lactobacillus casei* factor, the dosage of folic acid varying from 5 to 20 mgm. daily and the period of treatment from eight days to three weeks.

Three patients died of severe infections before the effect of the folic acid could be evaluated. In the remaining nine an unequivocal response was obtained, characterized by a reticulocytosis within a few days of starting treatment, a rise in the red cell count and haemoglobin level, and a return of the bone marrow picture to normal. No relapses were observed in a follow-up period of ten months.

Folic acid therapy gave completely negative results in 18 children with anaemia of prematurity, five with hypochromic microcytic anaemia, one with Mediterranean anaemia, two with chronic hypoplastic anaemia, one with subacute myelogenous leucaemia, one with acute lymphatic leucaemia, and one with sickle cell anaemia. In none of these patients was a reticulocyte response obtained, nor did improvement of the anaemia occur even when large doses of folic acid, up to 50 mgm. daily, were given parenterally. The prophylactic use of folic acid from birth onwards over a period of months in premature infants did not prevent the development of anaemia comparable to that observed in control patients. A combination of folic acid and iron therapy did not increase or accelerate the effect of the latter in cases in which iron was indicated. *F. Murgatroyd.*

WILSON, H. E., SASLAW, S. & DOAN, C. A. **The Effect of Folic Acid (*Lactobacillus casei* Factor) in Nutritional Hematopenia of Monkeys.** *J. Lab. & Clin. Med.* 1946, June, v. 31, No. 6, 631–42, 5 figs. [23 refs.]

DAVIS, J. E. **On the Mechanism of Action of Folic Acid and Liver Extract in the Treatment of Anemia.** [Correspondence.] *Science.* 1946, July 12, 37–8.

MERSKEY, C. & BASKIND, E. **Chronic Haemolytic Icterus resembling Acholuric Jaundice occurring in an African Native.** *South African Med. J.* 1946, May 11, v. 20, No. 9, 230–33.

An African native, complaining of pains in both legs attributed to osteitis of the tibiae, and with an enlarged spleen thought to be due to chronic malaria, was found on investigation to present features suggestive of acholuric jaundice. The erythrocyte fragility, tested by saline solutions, was increased, there was a slight reticulocytosis, a positive indirect van den Bergh reaction, and increased urobilinuria, without anaemia or evidence of haemolytic crises. Owing to lack

of facilities it was not possible to measure the mean corpuscular diameter, but in blood smears the cells appeared microcytic and dense, which together with a mean corpuscular volume not far removed from normal, was presumptive of spherocytosis. Some years previously the patient had had a severe illness lasting three months, during which he had had many small haemorrhages from his nose and mouth, and since that time he had had occasional febrile attacks. He had never noticed any jaundice, and such of his family history as was available, revealed nothing of significance. As he was free from symptoms he was discharged from hospital with a diagnosis of acholuric jaundice. He was subsequently twice admitted to hospital, and the haematological findings again supported this diagnosis. The illness which brought him to hospital for the third time was a characteristic haemolytic crisis. For the first time he showed an appreciable anaemia, and a well-marked reticulocytosis. The bone marrow was typically erythroblastic, and this reaction, as well as a leucoblastic irritation, could be detected in the peripheral blood films. During his crisis his red cell count dropped by nearly two million cells per cmm., with only a slight increase in jaundice. There was a doubtful report of malarial parasites being present in his blood, but this was not confirmed, no significant auto- or hetero-haemagglutinins or lysins could be demonstrated, and no lytic drugs had been given.

The question as to whether the disease represented a congenital or acquired type of acholuric jaundice is open to some doubt, but the comparative mildness of the condition is suggestive of the former. Against this, however, must be weighed the fact that the patient had probably been subjected to prolonged malarial infection which might have lead to an acquired haemolytic anaemia. The authors believe this to be the first case of chronic haemolytic icterus to be reported in an African native. *F. Murgatroyd.*

SEN, A. K. **Argemone Oil.** *Indian Med. Gaz.* 1946. Mar., v. 81, No. 3, 126–8, 1 pl.

Argemone mexicana is found practically everywhere in India, since it will grow wild and in poor soil. The seeds being abundant and cheap, they are used alone or with others as adulterants of mustard seed, and argemone oil, as an adulterant of mustard oil, is known to be one, perhaps the only cause of epidemic dropsy.

The author here describes three chemical tests for the oil, as used at the Bengal Public Health laboratory, Calcutta.

(1) The *Nitric Acid Test.*—Pure nitric acid is thoroughly mixed, by shaking, with an equal quantity of the oil. On being set aside for the layers to separate, the acid layer becomes red. When adulteration in small quantity, up to 1 per cent., is present the colour is yellow, and with increasing adulteration this deepens to orange and finally to red. Fallacies of this test are: Sesame oil gives a yellow colour and artificial colouring matter may have been added. The test is, therefore, to be recognized only as a preliminary one.

(2) The *Cupric Acetate Test.*—Five cc. of the suspected oil and 5 cc. of a known good oil are placed in two test-tubes; 1 cc. of glacial acetic acid is added to each and the mixture is well shaken. Next, 2 cc. of 3 per cent. cupric acetate in distilled water, dissolved by heating in a water-bath, are added and the whole well shaken to mix and placed in a boiling water-bath for 15 minutes, with frequent shaking to prevent separation of layers. In the control tube the copper solution is sky blue; if argemone oil is present it is greenish; with adulteration as high as 10 per cent. it is yellowish-green. This test is confirmatory of the nitric acid test and will detect adulteration of 0·5 per cent.

(3) The *Ferric Chloride Test.*—This test, as now used at the Bengal laboratory, is a modification of that of S. N. SARKAR described in 1941 [see this *Bulletin*,

1942, v. 39, 711.] The modifications and the reasons for them are considered in detail and those interested should consult the article ; they are not very great. The author claims that the test in its modified form is simpler than the original, that the crystalline precipitate is obtained with so small an adulteration as 0·25 per cent., and that the acicular crystals are specific for argemone oil.

H. Harold Scott.

VENOMS AND ANTIVENENES.

DUREN, A. Les serpents venimeux du Congo Belge. [**Poisonous Snakes of the Belgian Congo.**] *Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires.* (Collection in–8°.) 1946, v. 15, No. 5, 45 pp., 11 figs. on 5 pls. [12 refs.]

In his introduction the author remarks that the poisonous animals of the Belgian Congo are not of much importance, that accidents due to them are few, and hence, " the problems to which they give rise are negligible in comparison with those arising from pathogenic organisms, worms and insects." To stimulate interest and research he has, therefore, produced this brochure " as the field for study is virgin soil waiting for discoveries to be made." The present work is introductory in nature. Snakes of the Belgian Congo belong to five families, Typhlopidae ; Glauconiidae ; Boidae ; Colubridae and Viperidae. Next, he gives lists of Opisthoglypha and Proteroglypha Colubridae and Viperidae which are poisonous. Speaking generally, about one-third of the snakes in the Colony are dangerous ; of 724 captured at Stanleyville, 331 were *Boodon olivaceus*, 75 were *Chlorophis irregularis*, both aglyphous Colubridae, 220 *Causus rhombeatus* and 98 *Bitis nasicornis*, Viperidae. Then follow some notes on 12 species, their size, habitats, feeding habits and, after general remarks on the poisons of Colubridae and Viperidae, such as are found in all textbooks, he offers some observations on Congo species and the effects of their bites, both garnered from the reports of others. No original work is recorded.

This article would serve well as an introductory chapter to detailed investigation of the subject as stated in the title, and in his conclusions the author asks for information on the following three points : (1) Return of cases of poisoning and abstract reports on the symptoms ; (2) Geographical distribution of the poisonous snakes of the Belgian Congo ; (3) Study of the venoms of those most common or most dangerous with a view to preparing antivenenes.

H. Harold Scott.

POLSON, A., JOUBERT, F. J. & HAIG, D. A. **An Electrophoretic Examination of Cobra Venoms.** *Biochem. J.* 1946, v. 40, No. 2, 265–9, 8 figs.

SMITH, H. M. **Preliminary Notes and Speculations on the** *Triseriatus* **Group of Rattlesnakes in Mexico.** *Univ. Kansas Sci. Bull.* 1946, May 1, v. 31, Pt. 1, No. 3, 75–101, 23 figs. & 1 pl.

DERMATOLOGY AND FUNGUS DISEASES.

HAILEY, H. **Treatment of Creeping Eruption (Larva Migrans).** *Southern Med. J.* 1946, May, v. 39, No. 5, 371–2, 1 fig.

At a meeting of the Section on Dermatology and Syphilology, Southern Medical Association, Cincinnati, in November 1945, the author described four cases of creeping eruption treated by him with onion poultices.

The poultices were prepared by spreading white vaseline over a piece of gauze and adding finely grated onion in a thickness of about ½ to ¼ of an inch, the poultice being covered with waxed paper or some other impervious material. It was applied nightly for three to seven nights. In his limited number of patients, the treatment proved as satisfactory as the use of ethyl chloride in similar patients.

The author claims that this treatment has the advantage of cheapness and freedom from pain, as compared with ethyl chloride which had proved extremely painful.

In the discussion which followed, seven speakers quoted their experience in the treatment of larva migrans with such a variety of remedies as arsenicals, antimony compounds, chrysarobin, ethyl acetate, ethyl chloride and carbon dioxide snow.

These opinions confirm the well-known experience, to which the author himself testifies, that " the large number of treatments for creeping eruption is good testimony to the fact that a better one is greatly to be desired." [Whether that desire has been satisfied by the treatment described would require considerably more evidence ; and the author's report has been made in the hope that other dermatologists will attempt to determine its true value. He has in any case added one more remedy to the already lengthy list of measures adopted against this distressing condition.] *H. J. O'D. Burke-Gaffney.*

NOVACOVICH, G. G. **Observations and Data on Prevention of Poison-Oak Dermatitis.** *U.S. Nav. Med. Bull.* 1946, June, v. 46, No. 6, 811–19, 1 fig. [15 refs.]

The so-called Poison-oak is a species of Poison Ivy, *Toxicodendron diversiloba* ; though it has an oak-like leaf it is not related to the oak in any way. It contains an allergenic oleoresin, the same as that in poison sumac and Japanese lac trees. Injection of the antigen produces some degree of immunity, but not great. Oral administration gives better results ; though the immunity is temporary it lasts for 5–6 months. It was found that about 2 cc. of the oil diluted and administered over a period of 8–9 months was sufficient. One method was to give, as an initial dose, 0·5 mgm. of ether-extracted residue and gradually to increase till " at the end of 45 days the day's dose was 150 mgm."

Various antidotes and protectives were tried : chlorinated lime, antigas ointments, perborate ointment among them. The best was found to be 10 per cent. chlorinated lime in an ointment basis consisting of :—

Cetyl alcohol	35·1
Stearyl alcohol	5·3
Ceresin	3·5
Castor oil	20·8
Mineral oil	21·9
Duponal WA pure	1·7
Sodium perborate	10·0
Boric acid	0·7

It inactivates (or destroys) the toxic principle and is also usable prophylactically. *H. Harold Scott.*

WEIDMAN, F. D. & GLASS, F. A. **Dermatophytosis and other Forms of Intertriginous Dermatitis of the Feet. A Comparison of Therapeutic Methods.** *Arch. Dermat. & Syph.* 1946, Mar., v. 53, No. 3, 213–25, 1 chart.

" There is acute need for a satisfactory means for keeping the feet of fighting men in good condition, in which connection intertriginous dermatitis poses a large problem." " As to specific curative agents, dissatisfaction is general, particularly

in respect to the recurrences that are so notorious. Thus far, salicylic acid, iodine and chrysarobin are the anchors, but the last two, particularly chrysarobin, are capable of producing a chemical dermatitis and hence should be employed only under expert medical supervision." In view of the urgent need of better chemotherapeutic measures against foot ringworm the authors undertook a carefully controlled experiment in treatment of intertriginous dermatitis on 117 life-sentence prisoners in a penitentiary. Six preparations were tested, as follows: (1) "Cresatin-Sulzberger" (metacresylacetate), used at full strength; (2) boric acid foot powder (5 per cent. boric acid in talc); (3) ointment of benzoic and salicylic acids (3 per cent. salicylic and 12 per cent. benzoic acid in a petrolatum base); (4) "Iodolate" (iodocholeate) used as a 20 per cent. ointment as supplied by the maker; (5) "Pomeio" (potassium mercuric iodide in 1·2 per cent. aqueous solution); (6) "Zephiran chloride" (a mixture of alkyl dimethyl benzyl ammonium chlorides). All the medicaments were applied by the prisoners themselves according to mimeographed instructions, and the results were classified as "Cured", "Nearly cured", "Improved", "Stationary" and "Worse." Considering only the "cured" and "nearly cured" cases, two preparations stood out apart from all the others in effectiveness; these were cresatin and the boric acid foot powder—the foot powder being nearly as effective as cresatin. When the "improved" results were added to the "cured" and "nearly cured," the salicylic-benzoic ointment entered the picture, and all three preparations seemed to be about equally effective in causing improvement, with satisfactory results in about three-quarters of the cases. This suggests that while the salicylic-benzoic ointment is as effective as the other two preparations in bringing about clinical improvement, its action seems to stop short of cure; this tends to bear out the view, sometimes expressed, that the effect of salicylic acid ointments is merely to remove the superficial epidermal scales. The results from preparations 4, 5 and 6 were frankly disappointing, in fact, 28·5 per cent. of the patients treated with iodolate were rendered "worse," and in some of the cases severe reactions, even amounting to suppuration or chemical dermatitis, occurred.

The authors were not able to confirm the views of Lewis that *Trichophyton interdigitale* and *T. purpureum* cause distinctive lesions, and that lesions caused by *T. purpureum* are specially resistant to treatment. On the contrary, they obtained cures in 50 per cent. of the *T. purpureum* infections and in only 32·4 per cent. of the *T. interdigitale* infections. The *T. purpureum* infections were almost confined to men below middle age. *J. T. Duncan.*

GOMEZ, J. E. **Tokelau in Guatemala.** *Arch. Dermat. & Syph.* 1946, Mar., v. 53, No. 3, 243–8, 3 figs.

This paper gives a good account of the history and nomenclature of Tokelau disease (tinea imbricata), first described by William Dampier in the Philippines in 1686. In the South Seas the disease is associated with the warm and very humid climate of the coastal areas, but in Guatemala it occurs most frequently at distances of 80 to 170 kilometres from the sea coast and at an altitude of 3,000 to 9,000 feet. Clinically and mycologically the Guatemalan disease is similar to that of the South Seas; it is commoner in women than in men and the predisposing factors seem to be malnutrition and neglect of personal hygiene. Treatment, on the whole, gave only disappointing results except in the case of sodium iodoxyquinolinsulphonate, which showed considerable promise and merits further trial.

To obtain clear photographs of the lesions, the skin was rubbed with a compress saturated with 10 per cent. gentian violet, and the following day, after careful washing, only the diseased scales were found to retain the dye.

J. T. Duncan.

MOORE, M. & ACKERMAN, L. V. **Sporotrichosis with Radiate Formation in Tissue. Report of a Case.** *Arch. Dermat. & Syph.* 1946, Mar., v. 53, No. 3, 253–64, 3 figs. [Refs. in footnotes.]

In the lesions of sporotrichosis, *Sporotrichum schencki* is sometimes seen as a yeast-like cell or a small collection of cells surrounded by eosinophil, club-shaped bodies similar to those seen in actinomycosis and some other fungus diseases. The appearance in sporotrichosis is sufficiently rare to warrant publication of the case. SPLENDORE, who was the first to describe the appearance (in 1908), named the fungus *Sporotrichum asteroides*, believing it to be a new species, but the organism when studied in saprophytic life was found to be the typical *Sporotrichum schencki*. The club-bodies are probably formed by the host tissues, although the species or the peculiar strain of the fungus parasite may be a determining factor in their formation. *J. T. Duncan.*

WILLETT, F. M. & WEISS, A. **Coccidioidomycosis in Southern California: Report of a New Endemic Area with a Review of 100 Cases.** *Ann. Intern. Med.* 1945, Sept., v. 23, No. 3, 349–75, 8 figs. [33 refs.]

Unsuspected exposure to infection by *Coccidioides immitis* during military training of United States troops in desert areas of California, Texas, Arizona and New Mexico, has revealed hitherto unknown endemic areas of coccidioidomycosis. The diagnosis of infection rests chiefly on a routine use of the coccidioidin skin test; a positive reaction, occurring in a man on whom a previous test had given a negative result, being accepted as satisfactory evidence of recent infection. Although a majority of the positive reactors are symptomless, the authors were able to analyse the symptomatology of 100 cases of primary coccidioidomycosis, in four of which (all negroes) the disease progressed to the grave, disseminated form. *Fever* of some degree was present in 80 per cent. of the cases, and it lasted, on the average, less than a week; *chest pain*, usually aggravated by deep breathing or coughing, in 73 per cent.; *cough*, in 64 per cent., was almost invariably non-productive, but the transient appearance of *blood-streaked sputum* was noticed in 3 per cent.; *joint manifestations*, chiefly arthritis, in 8 per cent.; *erythema nodosum* in 4·4 per cent. and erythema multiforme in 2 per cent. (of 135 patients); *malaise*, a vague symptom, in 43 per cent.; *anorexia* was definite in 30 per cent.; *headache*, in 27 per cent., was of a generalized type, and was so severe, in some cases, as to justify spinal puncture; *chills* occurred in only 12 per cent.

The X-ray picture of the chest usually showed some degree of parenchymal infiltration, ranging from a minimal lesion to consolidation, often associated with hilar adenopathy and thickening, and sometimes a pleural exudate. Pulmonary cavitation was detected in 6 per cent. of the cases and was always a *late* complication of the *acute* stage; its typical thin-walled character becoming apparent only after resolution of the surrounding consolidation. The lesions of bone were well-circumscribed areas of destruction, with some tendency to bone proliferation and elevation of the periosteum.

Dermal sensitivity to coccidioidin is evidence of present or *past* infection. It is usually demonstrable in two to four weeks from the time of infection, and it persists for an indefinite time. The reaction is apparently specific, but it is absent in the earliest stages of the disease (two to four weeks) and in the state of allergy associated with severe disseminated disease. Eosinophilia is present in some degree, ranging from 5 to 18 per cent., in most cases during the initial few weeks of the disease. Serum tests are of particular value both in diagnosis and prognosis; a declining antibody titre being an indication of progressive recovery, while a persistently high titre for complement-fixation

suggests an unfavourable issue. As primary coccidioidomycosis is essentially a pulmonary infection, the examination of the sputum (when obtainable) offers a means of diagnosis. However, the spherules of *C. immitis* are difficult to detect, even in specimens of sputum cleared by caustic potash solution, and although the fungus was cultivated from the sputum of 61 per cent. of the present series of cases, it was found by microscopy in only 28 per cent.

For a more detailed analysis this important paper should be consulted in the original. *J. T. Duncan.*

TROPICAL ULCER.

WEBB, J. G. **Tropical Ulcers and Penicillin.** *Brit. Med. J.* 1946, July 13, 49–50.

It was to be expected that as penicillin became more widely available, it would soon be added to the already imposing list of remedies which have been given a trial in the treatment of tropical ulcers.

In this paper the author, describing the results of seven years' study of tropical ulcers in South China, claims a remarkable response on their part to treatment with penicillin. The claim is, however, based upon 10 cases only.

The aetiology of tropical ulcer is discussed, and the clinical stages are described. The author accepts the specificity of *B. fusiformis* [*Fusiformis fusiformis*] as a causative organism and its disappearance as a criterion of cure. Six of the ten cases also showed the presence of "mixed cocci". The age of the ulcers before treatment varied from 3 days to 6 months (in two cases, the ulcers had relapsed after primary occurrences of five months and three years respectively).

Penicillin was given locally, a solution of 500 units per ml. being applied on gauze twice daily; and by intramuscular injection of 15,000 units three-hourly up to a maximum of 90,000 units (except in mild cases).

Results were very good, the fever and inflammation subsiding in one to three days, when the ulcer presented a smooth granulating surface. Further treatment was similar to that of varicose ulcers. The time of final healing is not recorded. The author enters a plea for the widespread use of penicillin as it becomes available.

[HAMM and OUARY (this *Bulletin*, 1945, v. 42, 495) and MOREAU and OUARY (*ibid.*, 1946, v. 43, 378) described 18 and 19 cases respectively of tropical ulcer treated with penicillin with apparently very good results. It is a matter of some doubt whether the beneficial effects in all of these cases were due to elimination of the *F. fusiformis* or, as appears to be more likely, the destruction of the "mixed cocci". The treatment merits wide trial, which will no doubt be forthcoming as supplies of penicillin become available.]

H. J. O'D. Burke-Gaffney.

MISCELLANEOUS DISEASES.

MIRICK, G. S., ZIMMERMAN, H. M., MANER, G. D. & HUMPHREY, A. A. **Melioidosis on Guam.** *J. Amer. Med. Ass.* 1946, Apr. 20, v. 130, No. 16, 1063–7, 8 figs.

This paper describes two cases of melioidosis in American service men, developing after some six months on Guam. Both cases ran an acute course terminating fatally after five and seven days, respectively. At autopsy, miliary

abscesses were present in the lungs, liver, spleen and kidneys. *Pf. whitmori* was isolated from the blood stream on the 5th day of disease in the second case and from the visceral lesions in both cases *post-mortem*. These strains grew readily on the usual media, including Koser's citrate medium, under aerobic conditions. and produced acid but no gas from glucose and galactose in two days, lactose, mannitol, xylose, maltose, sorbitol and adonitol in six days, and sucrose in nine days; rhamnose, dulcitol and trehalose were not fermented. Ammonia was produced from peptone, nitrates were reduced to nitrites, methylene blue was reduced and catalase produced. Cultures of the organisms produced a typical Strauss reaction on inoculation into male guineapigs Systemic penicillin (a total of 200,000 units in the first case, the amount in the second being unspecified) was without effect, and laboratory tests showed that these strains of *Pf. whitmori* were insensitive to as much as 35 units of penicillin per ml. Growth of an inoculum of about 1,000 bacteria in tryptose phosphate broth was, however, completely inhibited by sulphadiazine in a concentration of 15 micrograms per ml. in 18 hours at 37°C. *S. P. Bedson.*

HERBUT, P. A. & KINSEY, F. R. **Transitory Pulmonary Infiltrations (Loeffler's Syndrome) in Rabbits.** *Arch. Pathology.* 1946, May, v. 41, No. 5, 489–502, 3 figs. [Refs. in footnotes.]

Löffler, when first reporting cases of what has since come to be known as Löffler's syndrome—eosinophilia with transitory pulmonary infiltration—stated that recovery took place in all, so that no examination of the pathological changes was possible, but it was thought that the lesion was "a specific tissue reaction probably produced by a variety of antigens and comparable to erythema nodosa [*sic*] of the skin."

The authors have carried out experimental work on rabbits, sensitizing them to horse serum by repeated subcutaneous injections, then exposing the trachea and instilling horse serum intratracheally, a single dose of 5 cc. in one group, 0·5 cc. hourly for 5–12 doses in one or two days in a second group. Systemic disturbance was slight, but by X-ray pulmonary infiltrations were seen which cleared in 1–2 weeks; the tracheal secretions contained eosinophiles and the submucosa of the trachea and bronchi was congested and oedematous and showed infiltration with eosinophiles, but there was no blood eosinophilia, as in human cases of Löffler's syndrome, and the lung infiltrations were more persistent. The authors conclude that "Löffler's syndrome is an allergic inflammation of the lungs and that one route by which the allergen invades is that of inhalation." [In view of the absence of eosinophilia and the longer persistence of pulmonary signs the condition produced in these experimental rabbits differs from Löffler's syndrome in man, and the conclusion is, therefore, hardly justified.] *H. Harold Scott.*

DENNISON, W. & EVANS, W. **Report of a Case of Multiple Idiopathic Haemorrhagic Sarcoma occurring in a West African Native.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, June, v. 39, No. 6, 521–2, 3 figs. on 1 pl.

VAIZEY, J. M. **Noma treated with Penicillin.** [Memoranda.] *Brit. Med. J.* 1946, July 6, 14.

A record of three cases in which penicillin was of great value.

VAN DER WALT, S. J. & STEYN, D. G. **Recent Investigations into the Toxicity of Plants, etc., No. XV.** *Onderstepoort J. Vet. Sci. & Animal Industry.* 1946, Mar., v. 21, No. 1, 45–55, 3 figs.

"Of the 18 plants investigated the following four plants were, according to the literature available to the authors, for the first time proved to be toxic: *Tetragonia Schenkii* Schinz., *Encephalartos Lehmanii* (E. & L.) Lehm., *Moraea trita* var. *foliata* N.E. Br., and *Schizocarphus nervosus* (Burch.) F.v.d.M.

"The toxicity of the pupae of *Melasina circophora* Meyr. was also investigated."

WAHI, P. N. **Needle Biopsy of the Liver. Technique and Diagnostic Application.** *Indian Med. Gaz.* 1946, Mar., v. 81, No. 3, 130–34, 7 figs. (6 on pl.)

A plea for the taking of small portions of liver tissue by means of the Vim-Silverman needle as an aid in the diagnosis of obscure liver conditions. The bleeding-time, clotting-time, prothrombin-time and prothrombin concentration are first determined as a routine, and any serious tendency to bleeding, passive congestion of the liver, suspected liver abscess or suppurative cholangitis are considered to be contra-indications for the operation. Vitamin K is injected intramuscularly if the prothrombin concentration is 50–70 per cent.; if lower than that the operation should not be done. It is also given to all patients with jaundice. The track for subsequent insertion of the needle is anaesthetized and the needle then is passed half an inch into the liver substance; the trocar having been withdrawn, the inner split-needle is passed into the cannula; then the outer needle is advanced over the split-needle, to compress the latter and secure the piece of tissue, and rotated once to cut the base of the core. With enlarged and palpable livers entry is made below the rib margin in front; otherwise at the 9th or 10th intercostal space in the mid- or anterior-axillary line.

Six cases are mentioned in which this biopsy examination assisted or confirmed clinical diagnosis and others are referred to, *e.g.* one of lardaceous disease in a tuberculous patient in whom the liver condition had been thought to be cirrhotic. *H. Harold Scott.*

GENERAL ENTOMOLOGY.

FAUST, E. C. **Modern Methods for the Control of Arthropod-transmitted Diseases.** *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 205–12.

DAVID, W. A. L. **Factors influencing the Interaction of Insecticidal Mists and Flying Insects. Part II. The Production and Behaviour of Kerosene Base Insecticidal Spray Mists and their relation to Flying Insects.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 1–28, 1 fig. [17 refs.]

The author uses the apparatus described in a previous paper [this *Bulletin*, 1946, v. 43, 679] to investigate production and behaviour of insecticidal spray mists. The following factors are discussed:—

(1) Those concerned with atomization of the spray:—Design and dimensions of the atomizing nozzle, spraying pressure and air/liquid volume ratio, viscosity, surface tension and the density of the spray liquid.

(2) Factors concerned with passage of spray droplets through the air :—Composition of the droplets, size of the droplets and the influence of evaporation, rate of fall of the droplets.

(3) Properties of the mist in relation to insects at rest or in flight :—Composition of the mists and their changes with time, contamination of motionless and flying insects, transit volumes of the latter.

In the experimental section, mists of different composition were sampled at various times after evolution. A quantity of kerosene or other oil, dyed with Sudan III, was sprayed into the cabinet, and samples were collected from the mist : (i) by a sintered glass funnel from which the dyed oil was recovered and measured colorimetrically ; or (ii) by a sliding impactor or a cascade impactor. The design of the slide impactor is described. These two impactors give indications of the drop-size distribution for all drops except the very smallest. The quantity of spray which fell to the floor was estimated by a glass plate from which the oil was washed and estimated colorimetrically.

The results showed that :—

(1) Increase in air pressure (7·5 to 20 lb./sq. in.) for atomization produces a mist with a larger proportion of small droplets, so that a smaller amount falls to the base in a given time.

(2) Pre-spraying of the chamber, at the rate of 180 cc./1,000 cu. ft., greatly reduced the evaporation of the droplets of kerosene, subsequently sprayed at 12·8 cc./1,000 cu. ft., and much bigger drops resulted. The theoretical saturation concentration of refined kerosene in air at room temperature is about 1,700 cc./1,000 cu. ft., so that the vapour slows down evaporation of droplets at quite a low fraction of the saturation value. Pre-treatment of this type with the non-volatile white oil " P31 " had no effect on the drop size of the subsequent mist.

(3) The mists produced by kerosene were compared with mists of the very volatile petroleum ether and the non-volatile oil P31. The first evaporates to a mist of extremely small particles, and only 5 per cent. is deposited on the floor after ten minutes, compared with 20 per cent. of kerosene and 70 per cent. of P31. The drops of the P31 are generally of larger range than those of kerosene. (All oils were sprayed at a spraying pressure of 12·5 lb./sq. in., and at the rate of 12·8 cc./1,000 cu. ft.)

The very fine droplets are too small to impact, but slip round the air-stream past a flying insect. Consequently, the mists of very small drops of insecticide dissolved in petroleum ether are less effective than the same quantity applied in kerosene. This difference is greatest shortly after spraying, before the kerosene droplets have evaporated to very small dimensions.

(4) The addition, to a kerosene spray, of 5 per cent. non-volatile oil does not greatly increase the amount falling to the base in ten minutes, but it does produce a mist of rather larger droplets. Consequently, it is more effective in killing flying insects (as shown by tests with *Aëdes aegypti*) since they pick up a larger dose of insecticide.

(5) An increase in the quantity of liquid sprayed, from the rate of 12·8 cc./1,000 cu. ft. to double or quadruple this amount, reduces the speed of evaporation of droplets and increases the proportion which falls to the base.

(6) By means of the sliding impactor, the drop size distribution of sprays can be measured. Half a minute after spraying kerosene, the drops range from 3 to 20 microns in diameter ; but these have all evaporated to less than 3 microns in four minutes. If, however, 5 per cent. non-volatile oil is added, many larger droplets (up to 13 microns) can be preserved up to four minutes.

J. R. Busvine.

McGovran, E. R., Fales, J. H. & Goodhue, L. D. **New Formulations of Aerosols dispersed by Liquefied Gases.** *J. Econom. Entom.* 1946, Apr., v. 39, No. 2, 216–19, 1 fig.

Tests of various liquefied-gas aerosol preparations against houseflies and mosquitoes were made in a Peet-Grady chamber. Aerosol formulae showing great improvement in toxicity over the original formula have been developed by increasing the non-volatile content. The original contained 2·4 per cent. non-volatile material; this can be increased up to 15 or 20 per cent., with improving efficiency. Above 20 per cent., however, the efficiency definitely declines. [This is probably because aerosols with low non-volatile content evaporate to minute particles, too small to impact on the insects. Increasing the non-volatile content enlarges the final size of the droplets and improves chances of wetting the insects. Above a certain size, however, the drops fall rapidly to the floor.] Improvements in formula can also be made by adding more sesame oil or other synergist, or by adding DDT or benzene hexachloride. Details of several effective formulae are given. *J. R. Busvine.*

Goodhue, L. D. & Riley, R. L. **Particle-Size Distribution in Liquefied-Gas Aerosols.** *J. Econom. Entom.* 1946, Apr., v. 39, No. 2, 223–6, 6 figs.

A method of determining the particle size of liquefied-gas aerosols is described. The aerosol is projected into a settling chamber from a hole in the middle of the base, and allowed to settle for two hours, on to slides coated with mannitan monolaurate, which is oleophobic and retains the oil drops as lenses. By various measurements, the volumes of drops which produce lenses of different sizes can be estimated, and the numbers of each size can be counted. Distribution curves of particle size are given for aerosols of different composition. The most effective concentration of non-volatile material seems to be about 15 per cent. From insecticidal tests it appears that drops of insecticide 2 to 10 microns in radius are the most effective in killing free-flying insects. *J. R. Busvine.*

Glasgow, R. D. & Collins, D. L. **The Thermal Aerosol Fog Generator for Large Scale Application of DDT and other Insecticides.** *J. Econom. Entom.* 1946, Apr., v. 39, No. 2, 227–35, 24 figs. on 2 pls.

Ordinary insecticide atomizers produce droplets of the order of 50 to 150 microns in diameter. The smoke generators employed for military purposes (screening) evolve drops of oil 0·5 to 0·75 microns in diameter, but by suitable modifications they can be made to produce larger drops. A suitable size for insecticidal use appears to be about 10 to 50 microns. The authors have made some trials of two types of thermal fog generator for control of insects. [Very few observations are given; the tests are described as "successful" etc., or "dead insects swept up for a week afterwards."] The two generators used in the trials were :—

(1) The Hochberg-La Mer type, which evolves droplets by the use of superheated steam; and

(2) The Todd Thermal Generator, which employs a temperature-controlled blast of hot air to atomize the insecticide.

Successful non-residual control of houseflies, mosquitoes, "punkies [gnats]", blackflies, stable flies, etc., was obtained by the use of an aerosol produced from 5 per cent. DDT in kerosene used at the rate of 0·2 lb. of DDT per acre. This

type of aerosol was also used in buildings for control of cockroaches and clothes-moth larvae, but the results are not clearly stated. *J. R. Busvine.*

SCHROEDER, H. O. & LINDQUIST, A. W. **Sprayers—for dispensing Concentrated Insecticides.** *Soap.* New York. 1946, June, v. 22, No. 6, 149–51 & 173, 3 figs.

Small compact sprayers, from $\frac{7}{8}$ to $1\frac{1}{2}$ inches in diameter and $4\frac{1}{2}$ to 14 inches in length, have been made for atomizing concentrated insecticides in household use. The sprayer plan consists of a cylindrical "liquid tank" containing the insecticide, carried in a compression cylinder which slides up and down over the liquid cylinder. At the base of the latter is a leather washer-valve

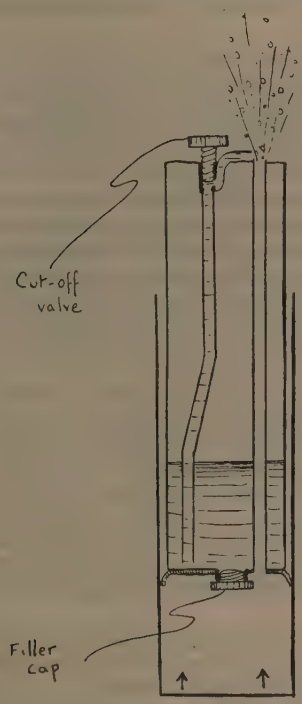

Diagram illustrating the essential details of the pocket size spray atomizer, redrawn in simplified form from figure 1 in the original paper by Schroeder and Lindquist in *Soap*.

in the centre of which is an oil resistant gasket for filling the liquid reservoir. The movement of the compression cylinder compresses air, which is carried up through a tube going right through the liquid tank. The liquid insecticide is drawn up by suction from another tube which runs to the base of the liquid cylinder, while the upper oriface is set at right angles to the air jet. The movement of the outer cylinder over the inner one thus generates the air to atomize the insecticide. When not in use, a screw valve in the liquid tube is closed to prevent leakage whatever the position of the apparatus. *J. R. Busvine.*

WIESMANN, R. & ZINKERNAGEL, R. Eine neue Methode zur Bekämpfung der Mückenbrut. [**A New Method of controlling Mosquito Larvae.**] *Gesundheit u. Wohlfahrt.* 1946, June, v. 26, No. 6, 297–332, 6 figs. [28 refs.]

Methods of controlling mosquito larvae are briefly reviewed, and the qualities of an ideal insecticide for the purpose are enumerated. The main body of the paper deals with experiments with "Gyron", a powder preparation containing 5 per cent. DDT compounded for larvicidal use.

Anopheles larvae in water that has been dusted with Gyron become restless in five to ten minutes; after fifteen to twenty minutes they frequently fall to the bottom and have difficulty in regaining the surface. Tremors begin and continue for a long time while the larvae finally are unable to leave the bottom. Similar signs of intoxication are shown by *Culex* larvae, but less rapidly since, owing to their position at the surface, they are less readily contaminated by the powder.

Pupae of both types of mosquito are resistant to DDT applied in this way. This is because the insect in this stage is protected by the cast skin of the last larval stage in which it is lying. There is one part of the body, in the abdominal region, where the new cuticle is still in contact with the old one. This part is sensitive to DDT, but normally is protected from the particles falling from the water surface because the abdomen is tucked under the body. If this position is disturbed, or if an emulsion of DDT is used, the pupae are killed.

From the outline area of the larva, the amount of active ingredient which falls upon it can be calculated. Thus it can be estimated that with a dusting of Gyron at 2 gm. per sq. m. a larva receives only 0·001 mgm. of DDT. This dose is sufficient to incapacitate all *Anopheles* larvae in about two hours and all *Culex* larvae in four hours. The speed of action depends on the temperature: experiments with *Anopheles* larvae showed that, with a dusting of 3 gm. Gyron per sq. m., all larvae sank in two hours at 18–25°C., in three and a half hours at 16°C., in six hours at 13°C. and in ten to eleven hours at 6°C.

In nature, it may happen that a pond dusted with Gyron will be cleared by the action of wind or rain after a certain period. Tests were therefore carried out to determine how long an exposure is necessary to result in the death of all larvae. Experiments were done at different temperatures, using 3 gm. Gyron per sq. m. in all cases. After various times under the toxic dust, the larvae were removed in a pipette to clean tanks. It was found that *Anopheles* larvae were killed by the following exposures to Gyron films:—20 minutes at 30°C.; 25 minutes at 25°C.; 35 minutes at 20°C.; 55 minutes at 15°C.; and 85 minutes at 10°C.

Experiments with various stages of larvae showed that the resistance increases with age from ffrst stage to fully grown larvae. The latter were accordingly used in most of the experiments.

Tests were made with Gyron to determine its effects on aquatic organisms other than mosquitoes. A normal dusting was harmless to newts and water snakes and also to Crustacea such as *Gammarus*, *Cyclops* and *Daphnia*. Of the insects, those forms which live on or visit the surface (water skaters, water beetles, etc.) were killed; though, surprisingly enough, the bugs *Nepa* and *Ranatra* were not affected when obviously contaminated.

Bottom-living forms were not harmed except in clean glass dishes, for they are normally protected by vegetation and detritus. Plants, coelenterates and protozoa were unaffected.

Comparative experiments were done with various other mosquito larvicides to compare them with Gyron. All were used at concentrations of 5 per cent. and applied at the rate of 3 gm. per sq. m. All were found to have some disadvantage; thus:—Paris green was effective but is poisonous to mammals,

etc. Phenothiazine (thiodiphenylamine) and hexachlorcyclohexane (crude Gammexane) are effective but soon lose their toxicity. "Gesarol", a horticultural preparation of DDT, sinks too quickly to the bottom. None was as satisfactory as Gyron.

Several small practical trials on still lakes with Gyron are described in some detail. It is concluded that it should be applied at the rate of 3 gm. per sq. m. and this will prevent breeding of mosquito larvae for three to four weeks. Therefore two or three dustings should suffice to prevent breeding throughout the summer breeding season. *J. R. Busvine.*

GOLDING, F. D. **A New Method of trapping Flies.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 143–54, 2 figs.

This new method consists of the use of "Até" adhesive, the coagulated latex of the vine *Carpodinus hirsuta* found in Nigeria. This latex is mixed with some vegetable oil, and produces the adhesive which is then applied to wires which are suspended in kitchens, etc. The fresh substance appears to attract the flies; after a week the viscosity decreases and many insects escape. [As a control measure this technique was of some value, but with the use of residual DDT it is probably already obsolete. It may be useful in making a survey of flies.]

Some interesting figures are given, showing the flies captured at Ibadan. Houseflies, mainly *Musca domestica*, were trapped over two years in 17 kitchens; In all 272,498 flies were counted. The maximum catch occurred during the summer rains, when the temperature was high and breeding accelerated, and when desiccation was not a serious problem to the flies. Flies were captured throughout the day, but in the greatest numbers at dusk.

Flies were also trapped in pig pens, where *Stomoxys* made up about 27·5 per cent. of the total catch. *Kenneth Mellanby.*

SMITH, A. & GREAVES, D. P. **A Case of Myiasis due to Warble-Fly Larvae.** *Brit. Med. J.* 1946, July 27, 120–22, 3 figs. [11 refs.]

A case due to *Hypoderma lineatum*, contracted in England.

MICHENER, C. D. **Observations on the Habits and Life History of a Chigger Mite, *Eutrombicula batatas* (Acarina : Trombiculinae).** Reprinted from *Ann. Entom. Soc. America.* 1946, Mar., v. 39, No. 1, 101–18, 34 figs. on 5 pls. [12 refs.]

This mite is of interest mainly because of its relationship to the Trombiculids which transmit scrub typhus. This paper contains no new information of direct medical importance, but various biological data are given which may assist those working on the disease-carrying mites. The life-history and its various stages are described in detail, and the duration of these stages is also given. The eggs, laid singly in damp soil, develop in about four days, but the larva remains another week in the shell; this is called the "deutovum". The active larva may take 14 days to find a host, on which it remains from two to ten days. It is active for up to four days after feeding, but then becomes quiescent, as a "protonymph." [This is often called the "nymphophane" by other authors.] This turns into the nymph, whose active life is from 16 to 45 days. There is another week of inactivity as a "preadult" before the final moult. The adult lives up to 45 days. The food of the nymph and adult has not been determined, but it is suggested that it may be fungal. The technique used is described. [For details see this *Bulletin*, 1946, v. 43, 797.] *Kenneth Mellanby.*

JAYEWICKREME, S. H. **A Note on the Breeding of Nymphs of the Trombiculinae (Acarina).** Reprinted from *Ceylon J. Sci.* Section B, Zoology. 1946, May 30, v. 23, Pt. 2, 95–6.

Scrub typhus research has always been held up because of difficulties in the handling and breeding of the vectors in the laboratory. So far no really satisfactory technique of breeding the Trombiculid mites has been described, though several workers have suggested that they have discovered improved methods which, on further investigation, show little advance. The author of the present paper is less ambitious in his claims, and only sets out to show how to obtain the nymphal stage from the larva, a step which has often been accomplished before, but not with the same high percentage of success. Engorged larval mites were kept in glass cells on wet cellulose wadding. The larval skins could usually be correlated with the nymphs which emerged, an important step in obtaining a correct description of the various stages in the life-history.

Kenneth Mellanby.

DE MEILLON, B. & DAVIS, D. H. S. *Pulex irritans.* [Correspondence.] *Trans. Roy. Soc. Trop. & Hyg.* 1946, June, v. 39, No. 6, 544.

In the flea survey of the Union of South Africa, *Pulex irritans* was found on rats and other rodents, dogs, a pig and a calf.

EDNEY, E. B. **An Apparatus for handling Small Living Insects.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 83–7, 3 figs.

This enables such insects as fleas to be sorted and examined, alive, under the microscope. With practice, an individual insect can be isolated ready to examine in 15 seconds. A suction pump, glass and rubber tubing, wax and Canada balsam are all that is required. For details of the mechanism reference must be made to the original paper, which cannot very well be summarized.

Kenneth Mellanby.

SWARTS, W. B. & WANAMAKER, J. F. **Skin Blisters caused by Vesicant Beetles.** *J. Amer. Med. Ass.* 1946, June 15, v. 131, No. 7, 594–5, 4 figs.

The author states that "more than 200 species of blister beetles have been found in the United States." The species depicted in this paper, *Epicauta cinerea*, is about 1·5 cm. in length, a deep purple in colour. The insect will crawl over the skin without doing any harm unless disturbed, irritated, or hindered by clothes; then its body exudes an irritating, blistering fluid, but the blistering does not appear for 24 hours or so, by which time the fact of contact may have been forgotten. The bullae it produces are round, dome-shaped, hemispherical, without any surrounding erythema. Opening to release the fluid and the application of a mild antiseptic bring about complete healing, without any scarring, in 10 days. Diagnosis has to be made from bullous dermatoses such as pemphigus, dermatitis herpetiformis, dermatitis venenata and inflammatory bullae from thermal or chemical agents.

H. Harold Scott.

LABORATORY PROCEDURES.

DE BURGH, P. M. **Notes on Field's Stain.** *Med. J. Australia.* 1946, Apr. 20, v. 1, No. 16, 544–5.

The author of this paper refers to some of the factors involved in the success or failure of Field's stain to produce good staining of the malaria parasite, principally in achieving a red chromatin dot and blue cytoplasm.

He discussed the drawbacks in the use of preparing modifications of Field's Solution 1, and describes a modification of McNeal's acid oxidation method used by LILLIE in preparing Giemsa stain, which was found satisfactory in preparing Field's first solution [this *Bulletin*, 1945, v. 42, 414; 1944, v. 41, 74].

DE BURGH also found erythrosin slightly preferable to eosin in Solution 2. He discusses the action of Field's stain at length, and draws particular attention to the fact that when the final layer of haemoglobin left in the blood-film becomes too thick, the chromatin appears blue-black. "The success or failure of the stain depends mainly on the thickness of the film." He points out that preliminary removal of haemoglobin can be done in a variety of fluids, none of which has any real advantage over distilled water. He describes a modification of technique which, whilst it involves little increase in staining time, extends the range of thickness of the films over which good staining may be obtained.

The paper contains a wealth of technical detail, and, in order to appreciate its considerable practical value, it should be read in the original.

H. J. O'D. Burke-Gaffney.

RATCLIFFE, A. W. **A Note on Staining Plasmodia.** *Science.* 1946, May 17, 630–31.

The author suggests that our conception of plasmodial staining reactions may be incomplete.

(1) Blood infected with *P. vivax* (produced clinical and typical smear-positive malaria upon therapeutic inoculation) smeared and stained with Wright's stain failed to reveal any parasites.

(2) Similar blood which showed numerous parasites in fresh unstained blood failed to reveal any parasites in stained smears.

(3) Smears of blood with numerous parasites (*P. vivax*) which stained readily when first smeared could not, after transportation (Texas to Indiana), be stained to show organisms of diagnostic acceptability.

The author suggests that the solution of the problem of staining these organisms might be helpful in "the ancient and recurring problem of smear-negative patients progressing to necropsy demonstration of plasmodia."

The *p*H of the buffer, age of smear and brand of stain are important factors which determine the quality of the result. Old smears require a lower *p*H and longer staining time, and alkaline buffer produces a dark [blue] smear while an acid buffer produces a red smear. The author's chief problem was failure to obtain (red) staining of the chromatin. "Despite the red cast with acid buffers, it was the blue which seemed to stain the nuclei of the leucocytes, rather than the azure components of the stain." It is recommended that azure staining of the chromatin is improved by using alkali as a preliminary bath rather than as a medium for the stain, and sodium carbonate and ammonium hydroxide were found to be satisfactory. Fresh smears may be given brief exposure to *p*H 8–9 after fixation, and old smears to a stronger alkali, but the exact concentration or time has not yet been determined? By bathing old films in strong alkali and subsequently staining for 24 hours in Giemsa or Wright's stain, satisfactory results can be produced. The possibility of shortening the period of staining by adding a penetrant such as Tergitol-7 is being investigated.

[It is well known that old unstained films are extremely difficult to stain satisfactorily. The blood corpuscles become very hard, and fixation is unnecessary even when watery stains (Giemsa) are used. Such films stain a deep blue. The reviewer has found that temperature is an important factor; old films kept at 50°F. stain better than do similar films kept at 80° or 90°F.]

P. G. Shute.

CHERMOCK, R. L. & MULLER, H. E. **Use of Wetting Agents in Histological Fixatives.** *Science.* 1946, June 21, 731–2.

On the grounds that the speed of penetration of a tissue fixative probably enhances its quality, the authors carried out a series of experiments in which three wetting-agents were added to carefully-prepared solutions of nine different standard fixing solutions. Sheep cerebrums and human liver were found to be useful test tissues, and pieces of these, one inch square, were placed in 250 cc. of each of the nine fixatives for 24 hours. They were then sectioned and the degree of penetration estimated grossly by the use of colouring agents. The preparations were then carefully studied microscopically. The fixative solutions employed were ; Zenker's, Carnoy's, Helly's, Bouin's, Allen's, Gilson's, Orth's, Vandegrift's, and 10 per cent. formalin. Each was modified by the addition of three aliphatic substances, known to have the quality of decreasing surface tension. The aliphatics used were: Tergitol-7 ; Tergitol-4 ; and Tergitol-08. These were all used in the ratio of three drops to 100 cc. of fixative. The authors found no correlation between the various fixatives, their *p*H, component ingredients, or supplementary Tergitol, and the degree of penetration or the quality of fixation, staining and shrinkage. They did find, however, that in the case of Allen's, Orth's, Vandegrift's and Zenker's fluids and also 10 per cent. formalin, Tergitol-4 improved fixation and staining. Tergitol-08 produced a similar result when added to Zenker's fluid.

"All other combinations of fixatives and detergents showed either no improvement or a decrease in the quality of fixation and staining."

H. J. O'D. Burke-Gaffney.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

INDIA. **Annual Report of the Public Health Commissioner with the Government of India for 1943 and 1944** [BOZMAN, C. A.]. 39 pp., 1 folding map. 1946. Delhi: Manager of Publications. [As. 8 or 9*d*.]

Like its predecessor this is a "combined and curtailed report" of health conditions in India during two years. In a pamphlet of 39 pages it is obviously impossible to deal with the subject in an adequate manner ; and in view of the extreme gravity of the health situation in India there is an urgent need for a comprehensive survey of recent developments in the public health field, for the purpose of forming a true appreciation of the present position, and a reliable forecast for the future.

The Report of the Health Survey and Development Committee set up by the Government of India in October 1943, to study the organization of health services in India, covers part of the ground, and among the recommendations contained in the report great emphasis is laid on the need for a special department, under a "Registrar General of Vital and Population Statistics," "to work independently of the Central Health Department, but in close co-operation with it," to study vital statistics for the whole country, and to "publish an annual report on the population of India, incorporating such information as is available regarding existing conditions and possible trends for the future." A similar organization for each province is recommended.

Reference to this matter has been prompted by the following statements in the first page of the present report. "Famine is of itself not a problem for health administrators since its occurrence is primarily dependent on the total

quantity of food available and facilities for its distribution. Health administrators are, however, vitally interested in any condition of famine, since, unfortunately, such is invariably associated with the appearance of epidemic diseases due to causes other than mere lack of food." These remarks illustrate very clearly the radical defect that exists in the public health organizations of most countries of the world. Health depends not only on the control of infection but also on the control of the equally important preventable diseases caused by inadequate nourishment; so that although health workers have not been provided with the means of controlling malnutrition they ought frankly to insist that all their efforts to prevent infectious disease must be fruitless unless nutritional disease is kept under control.

The number of deaths from famine in Bengal during the year ending April 1944, is estimated at over one million. In Madras Presidency during the same period the deaths were 176,827 in excess of the average for the previous five years, and in the smaller province of Orissa the excess deaths were 52,146.

The birth rate for British India has continued to fall; it was 25·13 in 1944. The causes of the progressive decline during the past five years need very careful consideration, and this matter is said to be receiving the attention that its importance demands.

Cholera vaccines were used on a very large scale in some provinces; nearly 19 million inoculations were performed in Bengal in 1944, and in Madras there were more than 8 millions in 1943. Cholera-phage was still being intensively used in Bihar in 1943, in addition to inoculation.

Few statistics are given to show the prevalence of the chief diseases, but among the general statements it is interesting to note that compulsory inoculation against plague was enforced in certain areas of the Punjab, and that in 1944 the Government of the United Provinces issued orders that "all major irrigation and hydro-electric projects, and all drainage schemes should be scrutinized by the Public Health Department before completion."

A welcome note of optimism is sounded in connexion with kala azar, of which it is stated that it "might easily be a considerable public health problem in the areas that it attacks," but that it "can be said confidently to be now being kept in check," through systematic treatment which, fortunately, is also an effective method of control.

More than half of the report deals in general terms with the activities of the central and provincial health departments, medical research, and the work of the voluntary organizations. *John W. D. Megaw.*

VAN HOOF, L. **Pathology of Belgian Congo during the War.** *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1946, June 15, v. 2, No. 11, 459–63.

SCOTT, J. A. **Health Problems of the Amazon Valley.** *Texas Reports on Biol. & Med.* 1946, v. 4, No. 2, 245–59, 1 map.

PASCALE, H. O clima e a doença. [**Climate and Disease.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1945, Sept., v. 10, No. 25, 7–30, 5 graphs. [15 refs.] English summary.

General remarks on the factors which go to make up climate and a discussion of the ways in which they influence the individual, the vector and the multiplication of the *materies morbi.* Charts are reproduced which sacrifice clarity from presenting too much on a page; for example, a single chart is used for demonstrating the seasonal variations over 15 years of eight different diseases

—measles, whooping-cough, diphtheria, smallpox, scarlet fever, mumps, meningitis and anterior poliomyelitis in Alabama and Mississippi and another for Massachusetts and Connecticut. [It will be seen that the application is very limited and therefore of interest to few. The whole is too condensed for a more detailed abstract and those sufficiently interested should consult the original.] *H. Harold Scott.*

HERMITTE, L. C. D. **Venomous Marine Molluscs of the Genus** *Conus*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, June, v. 39, No. 6, 485-512, 33 figs. on 5 pls. [Numerous refs.]

This is an article of great importance and value in closing a serious hiatus in tropical medicine—our lack of knowledge of poisonous marine molluscs. The author deals with stings by species of *Conus*, stings which are always painful, often serious and sometimes fatal. A finely reproduced plate illustrates five species known to sting man, and in an appendix is a list of reported cases of each: *Conus aulicus*, *C. textile* (two fatal cases among these), *C. marmoreus*, *C. tulipa* and *C. geographus* (three fatal cases).

Dr. Hermitte gives a detailed account of a case under his own observation in the Seychelles in 1932, the first to be reported as occurring in the Indian ocean; up to then all had been reported from the Western Pacific. A man, 32 years of age, picked up a specimen of *C. geographus* and was cleaning it when he felt a sharp sting. Turning it over he saw a "fine sharp needle" (a radular tooth) being retracted.

"The burning sensation soon gave rise to numbness, and within a few minutes he felt his left arm tingling and gradually becoming numb. Then, feeling his head getting 'queer,' he wisely decided to regain the shore and go home. I have used the word 'wisely' because within an hour the whole of his body was numb, his sight was impaired, he had marked dizziness and nausea, he became completely paralysed and could not move his limbs or sit up, and speech was difficult. Had this occurred while he was still in the water he might well have lost his life by drowning.

"After 5 or 6 hours he began to improve a little and asked to be taken to my surgery at Mont Fleuri on the main island of Mahé, 3 miles distant across the lagoon.

"The accident had occurred at 9 a.m. and he was brought by 'pirogue' (canoe) to my surgery at 6 p.m., having been carried to and from the boat in a long chair. He was still giddy and unable to stand, with a feeling of general weakness in all four limbs.

"On examination there was nothing to see at the site of the sting and there were no signs of hypersensitiveness such as urticaria. His knee reflexes could not be elicited but his pupils reacted normally to light and to accommodation. The pulse rate and respiration were normal; there had been no respiratory difficulty at any time or any rise of temperature as far as he could tell. When examined his temperature was normal.

"These were obviously symptoms of some form of neuro-toxic poisoning."

This poison paralyses the centres of voluntary movement, thus differing from the poisoning of stinging fishes which cause tetanus-like symptoms.

The author dissected specimens of the mollusc and the stages of dissection are described in minute detail and clearly shown by illustrations which will prove of much help to others desiring to carry out research into this question. With a view to finding out the nature of the poison he obtained more specimens, but on their reaching England the poison had disappeared, or at least was no longer active (the specimens had been kept in alcohol). This research will probably therefore have to be carried out in the tropics on the spot. The

source of the poison seems to be " the coiled tube previously regarded as the duct of the ' Gland of Leiblin ' " (which is not a gland at all). Appended to the article is a list of 30–40 species of *Conus* recorded from the Seychelles.

H. Harold Scott.

BOOK REVIEWS.

JENSENIUS, Hans. **Results of Experimental Resections of the Small Intestine on Dogs. (Experimental Enteroprival Sprue.)** [Translated from Danish by Hans ANDERSEN, M.D.] 275 pp., 42 charts & 69 figs. on 35 pls. 1945. Copenhagen : Arnold Busck, Nyt Nordisk Forlag & London : H. K. Lewis & Co. Ltd., 136, Gower Street.

This investigation was primarily designed to elucidate the pathogenesis of pernicious anaemia. At the time of the publication of Castle's researches, attention was devoted to the stomach, but since 1936, when preparations of the small intestine were found to possess an anti-pernicious-anaemia effect, investigations on the effects of resection of this portion of the gastro-intestinal tract were also made, but it was found that resection failed to produce pernicious anaemia.

The main purpose of this very thorough piece of experimental research has been to throw additional light on a symptom-complex resulting from extensive resection of the small intestine, including changes in the blood picture, in the absorption of intestinal contents, and in the central nervous system. The relation of the symptom-complex to the clinical picture in man, especially in sprue, was studied with special reference to pathogenesis.

Previous clinical and experimental investigations.—Most investigations appear to have been concerned with the *extent* of resection of the small intestine compatible with maintenance of life. This has varied from one-third to nearly the entire length, but most writers regard it as about two-thirds. On the whole, children or young adults withstand this mutilation better than persons of more advanced age ; much depends upon the pathological condition of the bowel.

There are three possible ways in which one may try to compensate for the loss of a large portion of the small intestine :—

(1) The diet may be increased in amount, especially in its caloric content ;

(2) It may be rendered more absorbable, poor in fat, but rich in carbohydrate ;

(3) From experimental studies it appears that the unresected portion undergoes compensatory hypertrophy with resulting increase in function. Such a result has not been proved to occur in the rest of the digestive tract, *i.e.* the stomach and colon. Physiological studies show that the capacity for fat absorption is greater in the distal than in the proximal portion of the small intestine, which suggests that the distal portion is more essential for the maintenance of life than the proximal.

The author's investigations.—The animals used in these experiments have been fairly big pups, about 3–4 months old. The experimental material consisted of 25 completed experiments : 15 with distal, 5 with proximal resection ; 4 with short-circuiting of the distal part of the small intestine ; and 1 with distal resection of small intestine and resection of half of the colon. In all, the operation involved two-thirds of the small intestine, and in three instances only with distal resection was $\frac{3}{4}$–$\frac{4}{5}$ of the gut removed. Measurements must be taken at the time of operation ; otherwise, owing to contraction, quite different values are obtained. All animals submitted to distal resection died.

The duration of the " spontaneous " uncomplicated course of illness in this experimental group varied from 60 to 299 days, averaging 144. Similar figures apply to the group with short-circuiting of the distal small intestine, although the average was 201 days. After proximal resection, three out of five dogs were unaffected by this treatment through an observation period of 299–322 days. After distal resection the course of illness in most of the experiments shows a stage of longer or shorter duration, with gradually increasing general debility, followed by very rapid aggravation of the dog's condition, and terminating fatally within a few days.

The symptoms dominating the clinical picture consist of loss amounting to $\frac{1}{3}$ to $\frac{1}{2}$ of the pre-operative weight, arrest of growth, emaciation, anorexia, thin or " mushy " stools, (usually light in colour and steatorrhoeic), disturbances of gait, coprophagy, sometimes skin changes and oedema.

No previous investigations have been published in which experiments were limited to resection of the jejunum and ileum in order to show the significance of the small intestine in the pathogenesis of anaemia. Anaemia has been an almost constant result of resection of the distal 2/3 of the small intestine, but generally it has not become pronounced till the latter part of the experimental period—from a few days to a couple of weeks before death.

In five experiments the anaemia was macrocytic, and a macrocytic tendency was found in two animals which did not show obvious anaemia. Not infrequently, macrocytic anaemia was accompanied by anisocytosis with flat distribution curve. On the other hand, there was no hyperchromia or poikilocytosis. The bone marrow was usually hypoplastic. In a few therapeutic trials no effect was obtained from parenteral administration of liver extract ; in one a moderate transitory effect was obtained by oral iron therapy ; none from a preparation of small intestine, but in one experiment a reticulocyte reaction and rise in haemoglobin occurred after parenteral nicotinic acid therapy. In five resections of the proximal 2/3 of the small intestine, three did not, and two did, result in anaemia ; in one of the latter pronounced hyperplasia of the bone marrow became evident. Four experimental short-circuits of the distal 2/3 of the small intestine all produced anaemia, but no macrocytosis.

In support of these findings, the author quotes from the literature 10 cases of anaemia in man following resection of the small intestine, in 7 of which it was of the pernicious type.

Further, 55 cases of macrocytic anaemia, in man, in the presence of intestinal stricture or anastomosis, have been recorded. In the former the anaemia is typically pernicious ; in the latter it is usually macrocytic, resembling sprue anaemia. In all forms of idiopathic steatorrhoea anaemia is pronounced, both in tropical and non-tropical sprue it is macrocytic and hyperchromic. whilst in coeliac disease it is generally hypochromic, though rarely macrocytic. In regional ileitis, and in a few other intestinal affections, macrocytic anaemia occasionally occurs.

When all other evidence on pernicious anaemia, and on the impossibility of producing it by experimental resection of the stomach and duodenum, is reviewed, the most plausible conception appears to be that there exists an independent anti-anaemic function of the small intestine.

Digestive function of the reduced digestive canal.—Previous clinical and experimental studies on the absorptive conditions of extensive resection of the small intestine show an increased loss of fat and nitrogen in the faeces. Fat absorption is the function most markedly affected. The percentage loss of fat increases with extension of the resection, but shows no relation to the length of the interval between the resection and absorption test.

The material comprised eight absorption experiments prior to operation, showing on an average a loss of nitrogen amounting to 4·75 per cent. and a loss

of fat amounting to 4·79 per cent. (from 1·5 to 8·5 per cent.) ; in 10 absorption tests after the operation, six were carried out after distal operations—namely, four after resection, two after short-circuiting—and all these six resulted in an increased loss of fat amounting to 30–45 per cent. in five experiments, while in one the increase was only slight. There was a normal or high degree of hydrolysis of the fat, decreased passage time, and only a slight increase in the loss of nitrogen. In this respect there is no definite difference between resection and the short-circuiting experiments.

Finally, four absorption experiments were performed on three dogs submitted to proximal resection : here the loss of fat was considerably smaller than after distal resection, though still somewhat increased, varying between 7·6 per cent. and 18·2 per cent. ; the degree of hydrolysis was normal and the nitrogen was even less affected than after distal operation.

Similar disturbances or intestinal absorption are encountered in sprue ; and this resemblance seems to show that the steatorrhoea of this disease may be explained as primarily due to impairment of the function of the small intestine. The difference between the absorptive disturbance after distal and proximal resection indicates that fat absorption is connected chiefly with the distal part of the small intestine.

Pronounced steatorrhoea in intestinal disease, therefore, indicates that the lesion involves the distal portion of the small intestine. A low blood sugar curve in the glucose tolerance test is characteristic both of idiopathic steatorrhoea and tropical sprue. In the present experiments 15 tests performed prior to operation showed a rise of 50–70 mgm. per cent. After distal operations 21 tests were performed on six dogs ; they showed wide variations in the blood sugar curve, but in three completed resections all showed a low curve. This outcome is regarded as supporting the view that it is due to decreased and slow absorption from the small intestine, but that it appears especially when the proximal part is affected.

By the alcohol test, achylia was demonstrated in four dogs only, all others showed preservation of the hydrochloric acid secretion throughout the experimental period, including the terminal anaemic stages. The conclusion is formed that achylia is not an indispensable intermediate condition for the production of macrocytic anaemia associated with damage to, or loss of, small intestine.

In histological studies of the central nervous system in these dogs, extensive degenerative changes were found in the nerve cells such as swelling, shrinkage, ischaemic cellular changes and others resembling " Nissl's severe ganglion-cell disease." Usually they were accompanied by glial proliferation. The changes were most pronounced in the cerebral cortex and in the Purkinje cells of the cerebellum, but they were also found in the base of the brain, brain stem and spinal cord.

The clinical picture.—Generally speaking, histological examination of the digestive canal revealed no definite abnormality. In some cases, slight evidence of chronic enteritis was found in the form of lymphocytic infiltration, atrophy of the intestinal mucosa and dilatation of the intestinal crypts. Some changes in the nerve cells of the plexus myentericus [Auerbach's plexus] were occasionally seen. In a few experiments the stomach showed atrophy of the mucosa of the fundus. In anaemia, haemosiderosis was present in the spleen, liver and bone marrow. Comparison between the experiments with distal and those with proximal resection showed that the appearance of anaemia, macrocytosis, neuro-muscular symptoms, diarrhoea, impairment of fat absorption, hypoplasia of the bone marrow and changes in the nerve cells are connected with distal resection, whilst changes in the skin, and a flat glucose tolerance curve, are chiefly associated with proximal resection. In the course and symptoms they

provoke, experiments with distal short-circuiting of the small intestine approximate those with distal resection.

The clinical picture, particularly after distal resection of the small intestine, shows many resemblances to that observed after stomach operations, but differs in the relative inconspicuousness of the skin changes and achylia; in fact, the clinical picture is more closely allied to sprue than to pellagra.

P. Manson-Bahr.

DE WILDEMAN, E. [Directeur honoraire du Jardin botanique de l'Etat, etc.]. **A propos de médicaments antilépreux d'origine végétale. IV. Des *Strophanthus* et de leur utilisation en médecine.** [An Account of Anti-leprotic Drugs of Vegetal Origin. IV. The Use of Species of Strophanthus in Medicine.] *Institut Royal Colonial Belge. Section des Sciences Naturelles et Medicales. Mémoires.* (Collection in-8°.) 1946, v. 15, No. 4, 70 pp.

No. IV of this series of monographs gives a comprehensive account of what is known of the numerous species of *Strophanthus*, in regard to the chemical constituents and their use in medicine. This genus includes 62 species, 21 of which are found in the Belgian Congo, whose distribution in that area is recorded. The chemical constitution of the active ingredients varies considerably, both in detail and in the quantities found, in different species. Only the following three have been extensively investigated, and as the strophanthins found in them differ materially in their solubilities and activities, and as different species are recognized as official in various countries, it is necessary to add the initial of the species of plant from which each is derived, when dealing with their use in medicine. Thus *Strophanthus gratus* yields strophanthin-G., which is official in Germany, France and the United States; *S. hispidus* yields strophanthin-H., as used in a number of European and American countries; and *S. kombe* provides strophanthin-K., which is used in England and many other countries. Strophanthin-K. is 30 times as soluble as strophanthin-G., and is less toxic; it has been, therefore, much used for intravenous injection in Germany, as it is excreted within 24 hours (against two days in the case of strophanthin-G.) and is therefore less cumulative and toxic than the latter.

The alkaloids and glucosides are found in the greatest strength in the seeds, but are also present in the roots and young bark. Their value in cardiac diseases, and as diuretics, is well known. Other diseases in which information is given of the use of preparations from these plants, by the indigenous peoples of Africa and others, include leprosy, tetanus, whooping cough, asthma, angina pectoris; they are used as anaesthetics in eye and ear affections, for venereal diseases, vermin in the head, rheumatism, and especially for poisoned arrows, for which last purpose they were formerly cultivated in West Africa. Their use in leprosy, by the Ibos (according to the late Dr. Oberdoerffer), was in the form of a decoction of roots or young bark, but no evidence is recorded in this book on any results of this treatment. This work, with its numerous references to the literature of strophanthins, will be of great value to those interested in this important class of remedies.

L. Rogers.

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